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#### KEY TO ABBREVIATIONS

br — book review  
c — correspondence  
cr — case report

e — editorial  
MMS — Massachusetts Medical Society  
me — medical epiphany

mr — meeting report  
ms — manuscript  
n — notice

o — obituary  
\* — original article



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OF THE MASSACHUSETTS GENERAL HOSPITAL  
ANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

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## MENTAL-HYGIENE CLINICS

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BOSTON

MENTAL illness and its related problems are matters for public concern. The community is very sensitive to matters of public health, but generally its interest does not include mental disorders, the greatest and commonest of all menaces. Epidemics of typhoid fever, scarlet fever, diphtheria, infantile paralysis and encephalitis promptly arouse the people and the public authorities to action for preventive and remedial steps, but mental illness,<sup>1</sup> which takes nearly as great a yearly toll in morbidity as all the above combined (72 per cent),<sup>2</sup> does not elicit more than casual notice. The lay public is not alone in this attitude of *laissez faire*. Professional men and women, including many physicians, do not appear greatly alarmed and, one can safely say, are not cognizant of the magnitude of this menace. Nevertheless it is responsible for the hospitalization of thousands of people each year in this country, and costs much in the way of grief, unhappiness and money. It is time that the people realized that this menace of mental illness is their problem. Much has already been accomplished by a handful of pioneers, but more widespread interest and action are necessary.

In this paper I shall not go into the history of the development of the methods applied to solve this problem, but shall emphasize one procedure that appears to offer great promise. It is generally agreed that there are three principal ways of attacking mental illness: hospitalization of the mental patient after full development of the illness and marshaling, in the hospital centers, the modern methods of care and treatment; prevention by reaching the maladjusted and the predisposed before the illness has reached the stage requiring specialized care and treatment in a mental institution; eradicating these disorders by prophylaxis or specific methods based on increasing the opportunities for research and the discovery of the etiologic factors.

Hospitalization is necessary for most of the well-established psychoses, and treatment is carried out in a satisfactory manner in most institutions; this alone is inadequate, however, as witnessed by the marked overcrowding of all mental hospitals.<sup>3</sup>

Should more hospitals be constructed, or should more buildings be added to existing ones? A hospital plant involves a minimum initial outlay of millions, \$5,000,000 being about the average figure for a 2000 bed hospital. The annual maintenance cost of such a hospital is approximately \$800,000. This is a tremendous burden on the taxpaying public, and an attempt should be made to find less expensive methods of controlling mental disease. It appears desirable, therefore, to slacken the pace of the building program, at least from an economical point of view.

The other two methods mentioned above offer much promise and involve only a small fraction of the cost of constructing and maintaining additional buildings. The expenditure for research in Massachusetts, as well as in other states, is very difficult to determine accurately, but it is most certainly a very small proportion of the total expenditures for mental illness. Research facilities should be greatly increased at strategic locations in hospitals that offer the best opportunities. All hospitals, however, should be given sufficient stimulus to make a contribution.

The purpose of this paper is to stress the value of the so-called "mental-hygiene clinics," including child-guidance and habit clinics. Much has already been done by the establishment of child-guidance and habit clinics throughout the country, particularly in Massachusetts. More adequate co-ordination of the clinic work should be fruitful of results. The significance of the early detection and treatment of the maladjusted cannot be over-emphasized, but it seems equally important to expand clinical facilities to include those people beyond the age of fourteen years at the period of their lives when the first obvious manifestations

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of mental disease become apparent. There is no definite evidence to prove that the behavior patterns as seen in the child-guidance and habit clinics lead to mental illness or are the prodromal symptoms.

The adult mental-hygiene clinic appears to offer the most practical value. I was connected with such a clinic sponsored by the Danvers State Hospital and operated at the Lynn General Hospital,

TABLE 1. *Types of Cases.*

DIAGNOSIS	No OF CASES
Psychoneurosis	127 (50%)
Neurasthenia	49
Psychasthenia	31
Anxiety state	15
Hysteria	12
Hypochondriasis	8
Mixed	6
Reactive depression	3
Psychasthenia, with pathologic sexuality	2
Neurasthenia, with mental defectiveness	1
Mental deficiency	14 (5%)
Mental deficiency	9
Mental deficiency, with psychotic episodes	3
Borderline intelligence, with psychotic episodes	1
Borderline intelligence, with neurotic traits	1
Manic depressive psychosis	11 (5%)
Depressed	10
Manic	1
Situational reaction	10 (4%)
Neurotic adolescent	9 (4%)
Epilepsy	8 (3%)
Epilepsy	5
Symptomatic epilepsy	2
Epilepsy, with psychosis	1
Dementia praecox	7 (3%)
Simple	2
Catatonic	3
Hebephrenic	2
Syphilis	5 (2%)
Cerebrospinal syphilis	2
Juvenile paresis	1
General paresis	1
? central nervous system syphilis (? epilepsy)	1
Psychopathic personality	5 (2%)
Psychosis, with cerebral arteriosclerosis	4
Arteriosclerosis	4
Mild neurotic tendencies	4
Epidemic encephalitis (parkinsonism)	3
Arteriosclerosis, with neurotic symptoms	3
Senile changes	3
Primary behavior problem	3
Chronic behavior problem in adolescence	3
Miscellaneous	24
Unclassified	8
Total	255

Lynn, Massachusetts. The clinic was held one-half day each week and was conducted by one psychiatrist and one psychiatric social worker. The services of a psychologist were obtained when needed. The appended statistics were compiled to point out the types of cases seen at the clinic and the probable factors involved, and to promote pertinent comments and constructive thoughts.

The total number of patients treated from 1929 to 1934, inclusive, was 255. The diagnosis most frequently made, as shown in Table 1, was psychoneurosis, 127 cases, or 50 per cent of the total, being so diagnosed. Fourteen cases, the next lar-

gest group, were diagnosed as mental deficiency, and 11 as manic-depressive psychosis. The diagnosis of situational reaction was made in 10 cases, and that of neurotic adolescent in 9.

It appears, then, that the so-called "functional" or psychogenic conditions comprise the bulk of the cases treated. It is well to note, however, that neurotic symptoms may sometimes be the early or incipient stages of more malignant conditions, such as dementia praecox. These cases, if properly handled, should not progress to the more malignant conditions. There is no way to determine whether or not this will be true of the series reported here, but thus far no case with neurotic symptoms has progressed to either dementia praecox or any other malignant condition.

Forty-seven definitely psychotic patients were also seen at the clinic, including 11 diagnosed as manic-depressive psychosis, 7 as dementia praecox and 5 as central-nervous-system syphilis. Of these psychotic patients only 2 were committed on clinical recommendation or otherwise. Commitment was recommended in another case diagnosed as manic-depressive psychosis, depressed type, because of the severity of the symptoms and the inadequacy of the supervision. This recommendation was not followed, and the patient finally committed suicide. Therefore, of 47 psychotic patients, 44 could be satisfactorily handled at home under clinical supervision and treatment. The majority of these patients would, without question, have been committed if clinical services had not been available. The cost of the hospitalization of this group of 44 patients represents thousands of dollars. It is estimated that the average weekly per capita cost in all the state institutions is approximately \$8.00.<sup>4</sup> The average hospital residence of a mental patient is roughly four years. Therefore, on the basis of these figures, the

TABLE 2. *Etiologic Factors.*

FACTOR	No. OF CASES
Economic stress and employment conditions	121
Marital and sexual difficulties	118
Childhood conflicts	116
Physical conditions	84
Social adaptation	26
Hereditary factors	18
Alcoholism	12
Psychic trauma	11
Low degree of intelligence	10
Personality difficulties	8
Religious factors	4

hospitalization of a patient for four years would cost \$1664, and the hospitalization of 44 patients on the same basis would amount to a total of \$73,216. This apparently represents the saving effected by a clinic very limited in its scope and personnel.

In considering the factors involved (Table 2),

it is noteworthy that only 18 cases, or about 7 per cent, showed heredity factors that could be uncovered by searching social-service investigation. Environmental factors were found to exist in the majority of cases. Economic stress or difficulty in employment was present in 121 cases, or 47 per cent of the total. The economic factor was not the only factor in most cases, and it is difficult to evaluate its relative importance. Physical condition or disease is another significant factor. It was found to be present in 84 patients. Again, its influence on the patient's mental condition is difficult to evaluate. Childhood conflicts of various types were present in 116 cases. These conflicts originated from an oversolicitous mother in 21 patients, unwholesome home in 20, friction between parents in 12, broken home in 11, and a neurotic mother in 11. It may be significant that in only one patient were hardships of childhood considered important. Marital and sexual difficulties were present in 118 cases. Maladjustments of this type are undoubtedly bound up with profound personality difficulties or defects that do not permit adult, mature adaptation. The enumeration of the factors within the home and involving intimate, interpersonal relations looms large in the production of maladjustment, neurotic manifestations and other abnormal mental reactions.

Some emphasis might be placed on the importance of the economic situation in the family circle. Economic stress interferes with the quality of the life of most individuals and of the family group. There is an uncertainty concerning the opportunity of securing the necessities and the niceties of life, and this involves their fundamental, instinctive demands. It impinges daily in a very definite way on the fullness of the life of the individual and interferes with his relations with his fellow men. During a century of industrialism, more emphasis has been placed on the importance of acquisition, and this, along with bla-

tant exhibitions of wealth, has created in the minds of the less fortunate a feeling of envy, dissatisfaction and insecurity. Wealth and economic independence acquired for their own sake, or for the power they endow, are surely not insurance against mental deviations, but they do permit a better and more healthful mode of living. Money, in another way of thinking, also permits indispensable initiatives and the expansion of individual activity. Innumerable frustrations can rightfully be laid at the door of economic inferiority. Gone are the times when people were satisfied with little and content to live submissively with the simple satisfactions that became their heritage. Their sense of relative values has become profoundly modified.

#### SUMMARY

Those responsible for the care of the mentally ill have been active in promoting the idea of early treatment of incipient and acutely ill patients to prevent much of the accumulation of chronic cases that require costly and prolonged hospitalization.

Specialized clinics of the type discussed in this paper, and institutions dealing primarily with acute material, such as the hospitals in the psychopathic system, appear to be worthy of considerable expansion.

A statistical survey is made of a mental hygiene clinic dealing with the diagnostic groups treated and the probable factors involved.

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## SO-CALLED "MESENTERICOPARIETAL HERNIA"

## Report of a Case

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THE following case of imprisonment of the small intestine, owing to a congenital defect in the mesocolon, is reported because of the rarity of the condition.

## CASE REPORT

F.R., an 8-year-old schoolboy, entered the Peterboro, New Hampshire, Hospital on August 1, 1939, complaining of severe abdominal pain. The family and past histories were noncontributory except for an indefinite history, extending back for more than a year, of poorly localized attacks of abdominal pain lasting from 1 to 3 hours and unaccompanied by vomiting, fever or evidence of infection.

During the morning of the day before admission, the patient rode horseback and appeared to be well. He refused luncheon and later refused his supper, but made no complaint until the night preceding admission, during which his sleep was restless and he complained of abdominal pain. The boy stated that he had had a stool during the afternoon before admission, but this statement could not be corroborated. By morning he was complaining bitterly of abdominal pain, which he referred to the mid-abdomen and to the right side. He did not vomit or complain of nausea. On admission the mouth temperature was 98.6°F., the pulse rate 70, and the white-cell count 4000 with 53 per cent polymorphonuclears. The local physical examination was made with difficulty, but his physician, Dr. Donald Clark, found tenderness in the right lower quadrant without other positive physical findings in the abdomen. Rectal examination revealed a large amount of inspissated feces and tenderness more marked on the right side.

Two enemas were administered and were returned with formed fecal masses. Pain appeared to be aggravated by the enemas, and the patient spent the morning in a knee-chest position, which he assumed because of pain. One examination of the urine was negative. At noon the white-cell count had risen to 12,000, and the polymorphonuclears had increased to 90 per cent. There had been no vomiting and no apparent nausea.

Shortly after 1 p.m., I examined the patient in company with Dr. Clark. The child was in bed in the knee-chest position, which could be altered only after great protest. He would consent to be on his left side with the lower extremities flexed on the abdomen, and with great difficulty he was persuaded momentarily to be recumbent with the legs extended. The mouth temperature was then 99°F., the pulse 64. The facies were expressive of pain, the skin was cool and clammy, but he did not appear to be in deep shock. The general physical examination was not remarkable. The abdomen was not distended, and there was no intestinal patterning or visible peristalsis. There was no muscle spasm, but there was excruciating tenderness throughout the right side of the abdomen, with no recognized point of maximum tenderness. Palpation of

the left side of the abdomen caused no pain. No masses were felt. Rectal examination was negative. During examination the child appeared nauseated but did not vomit.

Laparotomy was performed at 2 p.m. without a pre-operative diagnosis having been made.

Under avertin and ether anesthesia, an incision, which was eventually extended from the right costal margin to the pubis, was made and the peritoneum incised without incident. The omentum presented, and with it the large intestine, identified as the transverse and left colon. The stomach, liver and gall bladder were normal in appearance and position. A large, thin-walled, transparent hemispherical peritoneal sac occupied the greater part of the abdominal cavity. Through the sac, coils of intestine were visible. The sac was incised, exposing the small intestine, appendix and cecum. The exposed small intestine was slightly cyanotic, and there was a volvulus of 180° in a clockwise direction. This was reduced, with improvement in the color of the bowel. With the volvulus reduced, the entire small intestine lay anterior to the transverse colon and toward the right side of the abdomen. Further exploration, with the transverse colon and omentum elevated, revealed a defect in the mesocolon adjacent to the last part of the duodenum and ligament of Treitz. Through this defect, the small intestine appeared to have passed progressively, beginning with the jejunum and continuing until the appendix, cecum and ascending colon had also passed through the defect. By exerting traction,—first on the right colon, then on the cecum, then on the ileum and finally on the jejunum,—the small intestine was withdrawn until it came to occupy its normal position below and behind the transverse colon. With this accomplished, the color of the bowel was good, and it was possible to place the intestinal tract in its normal position. The cecum and ascending colon were unduly mobile, and the ascending mesocolon was represented by a peritoneal reflection from the right ilio-lumbar fossa.

These several manipulations were not accomplished without the expenditure of a good deal of time and handling of the bowel. It therefore seemed unwise to prolong the operation by seeking to determine the distribution of the blood supply to the bowel. The abdominal wound was closed without drainage, intravenous glucose was administered, and the child was returned to bed in good condition without evidence of shock and with a pulse of 110 and a systolic blood pressure of 104.

Convalescence was uneventful, and the patient was discharged from the hospital 12 days after operation.

By September 28, 1939, he had gained 6 pounds, had returned to school, and there had been no complaints referable to the abdomen. The report of an x-ray examination by Dr. E. C. Vogt on this date was as follows:

A flat abdominal film shows the kidneys to be normal in size and position. There are no abnormal masses or calcification.

The barium enema fills the colon easily and well. The

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colon is normal in contour, and it is in proper position. The cecum is rather low. There is no obstruction. Examination after evacuation shows complete emptying of the colon.

In a gastrointestinal series the esophagus appears normal. The stomach is medium in size and position and normal in contour and empties freely. The duodenum appears normal. Films taken at intervals up to 45 minutes very well delineate the small intestine which is normal in appearance. There are no obstructions or constrictions, and the position is normal. The mucosal pattern is well shown and entirely normal. The head of the biliary column at 45 minutes is at the hepatic flexure.

Impression: normal gastrointestinal tract.

On June 12, 1940, the patient entered the Children's Hospital (Boston). In the fall of 1939 he had complained of transient abdominal pain on several occasions. The pain was neither severe nor localized. He had been considered to have a good deal of gas. Otherwise he had been well and his schooling had not been interrupted. He was admitted to the hospital for abdominal exploration and closure of the aperture noted at the former operation.

On June 14, an operation was performed. Under ether and other anesthesia a transverse upper abdominal incision was made with division of both rectus muscles and the external oblique aponeurosis and retraction of the internal oblique muscle. This incision gave a very good exposure. The first abnormality encountered was a dense stringlike adhesion about 15 cm long running from the ileum to the transverse colon. This was ligated and divided. The inferior edge of the omentum presented as two layers that were not fused so that the omental bursa was open. The transverse colon and the omentum were displaced upward and the small bowel was packed away, exposing the root of the mesentery and the superior mesenteric vessels. Just below these vessels and directed upward to the right was a slitlike aperture approximately 2 cm in height. Through this aperture a No. 20 rubber catheter was easily passed for a distance of 15 to 20 cm. It went to the right and presented behind and lateral to the upper portion of the ascending colon just below the hepatic flexure. After this demonstration the catheter was withdrawn and the edges of the aperture described were roughened with gauze and then approximated with four interrupted fine silk sutures. Another adhesion running from a loop of ileum to the inferior end of the previous abdominal scar was divided. This adhesion was about 2 cm in width and was relatively vascular. The cecum was mobile and easily delivered and with it an extremely long but otherwise normal appendix. The mesoappendix was ligated and divided. The appendix was crushed at its base, ligated and removed with the cautery. The intestine was placed in normal position. The free edge of the omentum, which presented in two layers, was approximated by means of a series of interrupted sutures resulting in the closure of the omental bursa. The abdominal wound was closed in layers with out drainage. Interrupted black silk sutures were used throughout except for ligation of the appendiceal stump and for the peritoneal closure the latter being approximated by means of a continuous catgut suture. The patient was returned to bed in good condition.

Convalescence was entirely uneventful, and he was discharged on June 25.

He was seen on November 21, when he was in excellent health, had gained 8 pounds in the preceding 5 months and was actively engaged in schoolboy athletics.

Both wounds were solidly healed, and there had been no emphysema.

## DISCUSSION

The anatomic abnormality in this patient is explained embryologically by the imprisonment of the small intestine beneath the mesentery of the developing colon (Longacre<sup>1</sup>), and is not a hernia in the sense of the term that implies protrusion or evagination of the intestine from the celomic cavity. During the third stage of return of the intestinal tube from its temporary extrusion into the yolk sac—in the fifth to eleventh weeks of embryonic life—the mesocolon (in this case, the transverse mesocolon) may fail in part to fuse with the posteroparietal peritoneum. This affords opportunity for the midgut to be covered by or imprisoned behind the mesocolon and it is the mesocolon that presents the appearance of a covering or enveloping peritoneal sac.

Excellent clinical and anatomic descriptions are available in the recent American literature, and it appears unnecessary to reproduce them although it is desirable to refer to the sources. Historically, Neubauer<sup>2</sup> appears to have described the condition first; Treitz's<sup>3</sup> description in 1857 is classic, and the several allied conditions are often referred to as 'Treitz hernias,' since he believed that the intestine deepened and protruded into one of the several peritoneal fossas about the duodenum. Moynihan<sup>4</sup> published a monograph on the subject in 1906. Bender<sup>5</sup> suggested a developmental as opposed to an acquired mechanism, and Eisler and Fisher<sup>6</sup> and Bender<sup>6</sup> introduced the term mesentericoparietal hernia to replace Treitz and paraduodenal hernia (right and left) and to distinguish these anomalies from internal hernias, many of which bear no anatomic relation to the condition under discussion.

Two excellent papers, based on anatomic dissections,—one by Longacre<sup>1</sup> and one by Callander, Rusk, and Nemir,<sup>7</sup>—discuss the type of anomaly presented in the reported case. Both are fully and beautifully illustrated and serve to make clear the embryologic basis for a puzzling clinical picture. Longacre's bibliography is particularly complete. These papers, published respectively in 1934 and 1935, have been followed by numerous articles up to and including June, 1940.

Brynn<sup>8</sup> described the case of a nineteen-year-old girl treated successfully, and stated his to be the forty-third reported case of right paraduodenal hernia and the fifteenth patient to recover.

Emenheiser and Pankratz<sup>9</sup> reported on necropsy observations in a case of left paraduodenal hernia and Averbach<sup>10</sup> noted the successful treatment of a fourteen-year-old boy presenting findings very

similar to those of the patient reported in this paper.

Paul and Hill<sup>11</sup> commented on the autopsy findings in a three-month-old female and discussed the embryology from a viewpoint slightly different from those of the authors referred to above.

Halpert,<sup>12, 13</sup> in 1938 and 1939, reported post-mortem studies of a thirty-five-year-old woman with a right paraduodenal hernia and of a fifty-five-year-old man with a left-sided hernia, respectively. He states in the 1938 paper that he presents the forty-ninth confirmed case of right paraduodenal hernia.

Snyder<sup>14</sup> presented another case, not included by Halpert, of successful surgical reduction, but in this case, death followed forty-eight hours after operation. The patient was a man of fifty-one with extensive pulmonary tuberculosis.

Johns<sup>15</sup> reported a left transmesocolic hernia and emphasized the importance of a significant symptom—the pain, however severe when standing, is relieved when the patient lies down. His patient was a man of twenty-eight years.

Hansmann and Morton<sup>16</sup> presented the case of a fifty-eight-year-old cretin whose hernia occurred through the external leaf of the mesentery of the ascending colon, and reproduced the roentgenograms, with and without barium, after the cecum had become obstructed. These authors review the subject and give a bibliography but include hernias that were sequelae of abdominal operations involving the several mesenteries. They make the valuable observation, based on statistics, "that in most instances the stoma of intra-abdominal hernia will be found by lifting up the transverse mesocolon and exploring the paraduodenal region."

Developmentally the condition described is intimately related to and may present symptomatology similar to the extrinsic obstructions stressed by Ladd.<sup>17-21</sup> In these obstructions, owing to incomplete rotation of the colon and defective mesenteric development, there may be a volvulus of the small intestine and compression of the duodenum by the overlying and abnormally placed cecum and ascending colon. Haymond and Dragstedt<sup>22</sup> have also described anomalies of intestinal rotation.

For references to imprisonment of segments of the small intestine in apertures in the paracecal ascending colon, there are articles by Chamberlain<sup>23</sup> and by Cullen.<sup>24</sup> A third case (C. H. No. 223661), not reported but successfully treated by resection of part of the ileum, was operated on by Dr. T. W. Botsford at the Children's Hospital in August, 1939.

The patient reported here differs from others previously mentioned because the imprisonment

was by the transverse mesocolon rather than by the ascending or descending mesocolon, because volvulus of the small intestine was present, and because the terminal ileum, cecum and part of the ascending colon were imprisoned, as well as the jejunum and upper ileum, which have been reported before. These are not discrepancies, however, since in addition to either the ascending or the descending mesocolon, the transverse colon may fail to fuse to the posterior peritoneum. Furthermore, all the imprisoned bowel was, embryologically speaking, part of the midgut—that is, the part supplied by the superior mesenteric artery. The presence of volvulus of the small intestine is quite uniformly found in the anomalies described by Ladd.<sup>17-21</sup>

Longacre<sup>1</sup> summarized the evidence for the belief that such cases are congenital anomalies by pointing out the size and extent of the so-called "sacs," the absence of a definite neck, the absence of entering and departing loops, the absence of omentum in the sacs, and peculiarities in the blood supply that cannot be explained as acquired. In the present case the exigencies of operation prevented observation of anomalies of blood supply, but to Longacre's evidence may be added the imprisonment of essentially all segments of the intestine arising from the midgut, the defective mesenteric attachments and the volvulus, which also occurred in the undoubtedly congenital anomalies described by Ladd.

Clinically the condition, although rare, bears an intimate relation to other forms of intestinal malrotation and reverse rotation that may produce obstructive phenomena in the newborn or later in life. It may also be the cause of symptoms similar to those produced by internal herniations into apertures in the broad ligament and omentum, and by incarceration of knuckles of bowel into the several pericecal and paraduodenal fossas.

It appears from the data reported that cases of this type are congenital anomalies of development of the intestinal tract, that they may exist without producing functional disturbance, that they may be responsible for long-continued but vague symptoms of disturbed intestinal function, and that they may produce acute obstruction phenomena, with varying degrees of circulatory impairment of the bowel. Andrews<sup>25</sup> states that the treatment of strangulation appears to be almost hopeless, reduction being nearly 100 per cent unsuccessful. He adds that unless strangulation takes place, the bowels are able to function normally.

About 50 cases of so-called "herniation" into the right mesocolon have been reported, about 150 into the left, and 2 into the paracecal segment of

the right colon; the present case is considered to be imprisonment by the transverse mesocolon.

Correct preoperative diagnosis is seldom possible, a total of 5 having been reported by Abrazon, von Haberer, Vautrin and Slandenmeyer (Longacre<sup>1</sup>). The use of x-ray examination has been suggested, and Snyder's<sup>14</sup> patient did present an appearance suggestive of incarceration of many loops of intestine. The existence of a tympanitic circumscribed mass has been described, but apparently has not been found in most cases. The usual symptoms are those of intestinal obstruction with varying degrees of shock. Pain appears to be the most constant symptom, and together with abdominal tenderness, may be the indication for operation. In this connection, one can do no better than to quote with Chamberlain<sup>23</sup> the statement of Mason and Atkinson<sup>26</sup>. "Time spent in differential diagnosis is ill spent. The decision to be made is whether or not the condition is surgical. The chagrin of the surgeon who operates and fails to find a surgical condition is nothing to that of the surgeon who does not operate in time."

Successful treatment postulates early operation before serious circulatory disturbances have developed, and a reasonably accurate knowledge of embryologic development so that a rational plan for relieving the intestinal obstruction and the vascular obstruction may be employed.

#### SUMMARY

A case of imprisonment of the segments of the intestine arising from the midgut by a congenital anomaly of the transverse mesocolon is presented, it is believed, for the first time; the successful surgical management of the patient is described.

The embryologic explanation for the anomaly is briefly described, and references are given to the descriptions of the related anomalies of so-called "herniations" into or imprisonment by the ascending and descending mesocolons. The clinical

and anatomic relations to other forms of faulty rotation and attachment of the colon are discussed. Additional evidence for the developmental basis for such anomalies is added—namely, the imprisonment of essentially all the intestine arising from the midgut, the defective mesenteric attachments and the coexistent volvulus of the small intestine. The designation of "hernia" is retained, since it is a useful and convenient term, although the anomaly is not a hernia in the usual sense.

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## GALLSTONES IN PATIENTS UNDER THIRTY YEARS OF AGE

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ALTHOUGH approximately 10 per cent of the population have gallstones,<sup>1</sup> the prevalence of this condition in patients beyond forty years of age has obscured its relative frequency in young persons. An analysis of 300 consecutive cases of operation for gall-bladder disease, including non-calculous cholecystitis,<sup>2</sup> disclosed that 21 per cent of the patients were under thirty years of age. It has been suggested<sup>3</sup> that if routine cholecystography were carried out in young persons, biliary-tract disease would be found even oftener.

In the present study of 232 unselected patients operated on for gallstones, 48, or 20 per cent, were under thirty years of age. There were 3 males and 45 females. The males were in their third decade, as were 41 of the females. The remaining 4 females were operated on before their twentieth year, the youngest being fourteen years of age.

Previous acute infections, including the exanthematous diseases, have been suggested as etiologic factors in the formation of gallstones in young persons. Twenty-seven patients (56 per cent) gave a history of one or more of these infections. Measles was the commonest, and whooping cough and scarlet fever were next in frequency. There were several cases of typhoid fever, chicken pox and mumps, 1 of smallpox and malaria, and 1 of influenza.

More than 50 per cent of all patients with gallstones have been reported to be obese,<sup>4-6</sup> but only 21 per cent of these young patients were overweight; 11 per cent were thin, and 68 per cent were of normal weight.

The symptoms were no different from those in other age groups. Although all these patients had pain to some degree, only 18, or 38 per cent, at times required morphine by hypodermic injection. In comparison with reports for older patients, nausea and vomiting (in 40 per cent) were approximately as frequent, but eructations (in 18 per cent) were about one fourth as common. In 6 patients (13 per cent) jaundice was present at the time of operation or had been observed during previous attacks.

The duration of symptoms varied from one day to seven and a half years (Table 1). The average was one year and eleven months, approxi-

mately four years less than the average for patients of all ages.<sup>7, 8</sup>

Approximately 70 to 90 per cent of women operated on for gallstones have symptoms in relation to pregnancy<sup>9</sup>; of the 36 married women in this

TABLE 1. *Duration of Symptoms.*

DURATION	NO. OF CASES
Less than 1 yr	15
1 to 2 yr	11
2 to 5 yr	17
Over 5 yr.	4
Unknown	1
Total	48

series, 18 (50 per cent) had attacks during the gravid state. The frequency of attacks during and shortly after gestation has been attributed to hypercholesterolemia, impairment of gall-bladder function and constipation. One patient, aged twenty-eight years, had attacks of pain so severe that the gall bladder was removed during the fourth month of pregnancy. She had an uneventful convalescence and no further symptoms during or subsequent to her pregnancy and confinement.

Six patients (13 per cent) had acute cholecystitis in addition to cholelithiasis. Four had symptoms for two months or less; the remaining 2, one and a half and seven and a half years, respectively. The gall bladders were viable, although in 1 case the mucosa was gangrenous. The fact that the symptoms did not exceed eight weeks in 4 of these patients indicates that acute cholecystitis in young persons may occur early during the course of cholelithiasis.

The common duct was opened and explored in 8 cases; stones were found in 3, an incidence of only 6 per cent for the series. These patients, whose ages were between twenty-four and twenty-seven years, had symptoms from four to seven years; none were jaundiced at the time of operation, and only 1 gave a history of jaundice. As in older patients, the longer the duration of symptoms, the greater the incidence of this complication.<sup>10</sup> For patients of unselected ages, 16 to 21 per cent are estimated to have choledocholithiasis,<sup>11, 12</sup> with jaundice in 60 to 91 per cent.<sup>12, 13</sup>

Three patients (6 per cent), who were twenty-six, twenty-seven and twenty-nine years of age, respectively, had acute pancreatitis in addition to

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cholelithiasis. One had edema of the pancreas, and the other 2 had hemorrhagic pancreatitis with fat necrosis. One was operated on within twenty-four hours of the onset of the first gallstone attack, and the others had biliary symptoms for one and three years, respectively. It is therefore obvious that young patients with gallstones can have acute pancreatitis as an early complication.

There were no deaths in the series. The gall bladder was removed in each case, and, as already mentioned, the common duct was opened and explored in 8. Thirty-eight patients (79 per cent) also had an appendectomy, including 7 who had additional surgery.

Forty-six patients (96 per cent) had an uneventful convalescence and were discharged from the hospital within two weeks of operation. One of the remaining patients was in the hospital thirty-five days because of a phlebitis, first of one leg and then of the other. The second patient, whose common duct was drained, had a nonvirulent gas-bacillus infection necessitating twenty-one days of hospitalization.

It has been possible to follow 38 patients (79 per cent) for a period of one to fourteen years. Only 2 have thus far complained of subsequent distress. One patient had epigastric discomfort two years postoperatively; roentgen-ray examination revealed a duodenal ulcer. The other, after being free from symptoms for four years, had an attack of epigastric pain that persisted for several days. Careful investigation, including a gastrointestinal roentgen-ray examination, was negative. Whether the recurrence of pain in this patient was due to an overlooked common-duct stone or to an extrabiliary condition has not yet been determined. The 3 patients who had stones removed from the common duct have been free from symptoms for two to four years.

## SUMMARY

Of 232 consecutive operations for cholelithiasis, 48 (20 per cent) were on patients under thirty years of age. The average duration of symptoms was one year and eleven months.

In addition to cholelithiasis, 6 patients (13 per cent) had acute cholecystitis, 3 (6 per cent) had acute pancreatitis, and 3 (6 per cent) had stones in the common duct.

The gall bladder was removed in each case. There were no deaths, and postoperative complications occurred in only 2 patients.

Of the 38 patients (79 per cent) who have been followed for more than one year only 1 developed symptoms that might have been related to the biliary tract, and these occurred four years after operation. There has been no recurrence of symptoms in those who had common-duct stones.

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# MASSACHUSETTS MEDICAL SOCIETY

## PROCEEDINGS OF THE ONE HUNDRED AND SIXTIETH ANNIVERSARY

THE one hundred and sixtieth anniversary of the Massachusetts Medical Society was observed in Boston on Wednesday and Thursday, May 21 and 22, 1941, at The Copley-Plaza.

### WEDNESDAY, MAY 21

A general clinical meeting was held in the Sheraton Room in the forenoon, under the chairmanship of Dr. Bennett F. Avery. The attendance was approximately 425.

The supervising censors met in Parlor A at 10:00 a.m., and the Council convened in the Swiss Room at 10:30 a.m., the Cotting Luncheon being served at 1:00 p.m.

During the noon hour, the sections met for a series of round-table discussions and luncheons, at which the new officers were elected. The Section of Medicine met at the University Club, with an attendance of 148; the Section of Obstetrics and Gynecology at the University Club, with an attendance of 77; the Section of Surgery in the State Salon of The Copley-Plaza, with an attendance of 85; the Section of Pediatrics at the Hotel Lenox, with an attendance of 56; the Section of Dermatology and Syphilology at the Hotel Lenox, with an attendance of 53; the Section of Radiology and Physiotherapy at the Hotel Lenox, with an attendance of 13; and the Massachusetts members of the New England Society of Anesthesiology at The Copley-Plaza, with an attendance of 35.

In the afternoon, a general clinical meeting was held in the Sheraton Room, Dr. C. Sidney Burwell presiding. The attendance was around 450.

That evening, the annual dinner was held in the Sheraton Room, 281 members and guests being present. The president, Dr. Walter G. Phippen, introduced the delegates from the medical societies of the other New England states, as follows:

MAINE: Dr. Theodore E. Hardy, Waterville

NEW HAMPSHIRE: Dr. Clinton R. Mullins, Concord  
Dr. Leslie B. Copenhaver, North Woodstock

VERMONT: Dr. Michael F. Cerasoli, Barre

RHODE ISLAND: Dr. Charles A. McDonald, Providence  
Dr. Joseph C. O'Connell, Providence

CONNECTICUT: Dr. Charles H. Turkington, Litchfield

Dr. F. Erwin Tracy, Middletown

After short speeches by Drs. Nathan B. Van Etten and Frank H. Lahey, president and president-elect, respectively, of the American Medical Association, the attending fellows adjourned to the Swiss Room, where Dr. E. W. Alton Ochsner, of New Orleans, delivered the Shattuck Lecture, his subject being "Thrombosis and Thrombophlebitis." (This lecture will appear in the July 31 issue of the *Journal*.)

### THURSDAY, MAY 22

A symposium on hormones was held during the early forenoon, under the chairmanship of Dr. Charles E. Mongan; the attendance was approximately 425.

### ANNUAL MEETING

The one hundred and sixtieth annual meeting was called to order by the president, Dr. Walter G. Phippen, in the Sheraton Room at 11:00 a.m. Approximately 400 were in attendance. The minutes of the previous annual meeting were approved as published in the July 4, 1940, issue of the *New England Journal of Medicine*. The Secretary *pro tempore* then presented the changes in membership, as follows:

Membership reported May 22, 1940 ..... 5542

#### Losses

Deaths	104	
Resignations	17	
Deprivations	49	
	—	170

#### Gains

New fellows	238	
Readmitted by censors	1	
Restored by Council	28	
	—	267

Net gain . . . . . 97

Membership reported May 22, 1941 . . . . . 5639

Proposed changes in the by-laws, which had previously been approved by the Council and copies of which had been forwarded to all members of the Society, were then considered. Dr. Phippen called attention to the fact that the last

four proposed amendments had been inadvertently omitted from the notice of the annual meeting and that a postcard calling attention to the omission had been sent to every member. The amendments were considered in order, and were accepted without change, except that in Amendment 17 the word "Society" in the next to the last line in the first paragraph was changed to "Council". The amendments, as accepted, were as follows:

**AMENDMENT 1** Amend Chapter I, Section 1, to read

Applicants for admission to fellowship in the Massachusetts Medical Society are required to satisfy the censors that they are not less than twenty-one years of age, that they are of sound mind and of good moral character, that they possess a good English education, that they have received a diploma from a medical school or college recognized by the Council, or that they have, in each instance, received the approval of the Committee on Medical Education, that they do not practice medicine in a manner contrary to the code of ethics of this society, that they have made application according to the provisions of Chapter V, Section 2, that they have paid the examination fee of three dollars and they shall appear personally before the censors and satisfy them that the above requirements are fulfilled.

**AMENDMENT 2** Amend Chapter I, Section 6, to read

Fellows shall be assessed annually such a sum as the Council may determine. The fiscal year shall begin on the first day of January. Assessments shall be payable in advance. The first assessment paid by a fellow admitted to the Society following the December examinations shall cover his dues for the succeeding fiscal year and shall be the amount fixed for that year.

**AMENDMENT 3** Amend Chapter I, Section 7, to read

The resignations of fellows whose assessments have been paid in full or remitted, may, on recommendation of the Committee on Membership, be accepted by the Council. Petitions to be allowed to resign should be sent to the treasurer of the general society.

**AMENDMENT 4** Omit the last paragraph of Chapter I, Section 9.

**AMENDMENT 5** Add in Chapter I the following

**Section 10** Former fellows who desire to be re-admitted to the Society shall make application in writing addressed to the Council and sent to the secretary of the Society. Such applications shall be referred for investigation and personal interview to the local boards of membership, which shall report their recommendations to the Committee on Membership. The committee shall render the final decision as to whether to recommend to the Council the readmission of former fellows. The Council shall have the power to readmit former fellows so recommended. Boards having under consideration the applications of fellows whose resignations have been requested by the Committee on Ethics and Discipline, or who have been deprived of fellowship under the terms of Section 8, Clause (c), shall consult with the Committee on Ethics and Discipline before reporting their recommendations.

**AMENDMENT 6** Add to Chapter III, Section 5, the following

The councilors of each district society shall meet at or as soon as possible after the annual meeting of the district society in 1941 and elect one of their number to serve as a member of the Executive Committee of the Council, in accordance with Chapter IV, Section 10. Thereafter, in a similar manner, they shall elect a new member from time to time.

**AMENDMENT 7** Add in Chapter III, Section 7, the following

The secretary of each district society at or as soon as possible after the annual meeting of the district society and before the annual meeting of the general society in 1941 shall call together its councilors for the purpose of electing a member of the Executive Committee of the Council and shall send the name of the member chosen to the secretary of the general society. He shall see that a new member is chosen in a similar manner to fill a vacancy as it occurs, in accordance with Chapter IV, Section 10.

**AMENDMENT 8** Add to Chapter IV the following

**Section 10** The Executive Committee shall consist of the President, President Elect, Vice President, Secretary and Treasurer *ex officio*, and a councilor from each district medical society chosen in accordance with Chapter III, Section 5.

The councilors of each district society shall meet at or as soon as possible after its annual meeting in 1941 as specified in Chapter III, Section 5, and in a similar manner at stated intervals as specified below, to choose one of their number to serve as a member of the Executive Committee of the Council.

A member of the Executive Committee shall serve for three years and shall not be eligible for re-election before the expiration of three years following the conclusion of his term of office except that in the first year of operation six members shall be selected by lot to serve one year, six members shall be selected by lot to serve two years and six members shall be selected by lot to serve three years. Thereafter six members shall be elected every year to succeed in office those whose terms are about to expire.

The Executive Committee shall meet at the call of the President at least once in each interval between Council meetings and may meet more often at the pleasure of the President. It shall assist the President in preparing for the consideration of the Council matters calling for action by the Council at its next meeting. It shall authorize action by the officers of the Society when circumstances require it subject to the approval of the Council. It shall perform such other duties as the Council may require.

An executive secretary may be chosen by the Executive Committee upon nomination by the President.

Upon request members of the Executive Committee shall be paid the amount of their traveling expenses from the funds of the Society.

**AMENDMENT 9** Amend Chapter V, Section 1, to read

The supervisors representing the censors of the several district societies, shall constitute a board which shall meet annually on the day appointed for the annual meeting of the Council. The board shall elect a chairman, who shall have power to call special meetings. Five supervisors shall constitute a quorum. The secretary or executive secretary of the general society

shall act as secretary of the board. He shall call special meetings at the request of five supervisors. He shall keep a permanent record of the proceedings of the board, and shall provide, at the expense of the Society, papers and forms necessary for conducting examinations of applicants for fellowship. The board at its annual meeting shall adopt a uniform plan for the examination of applicants. The supervisors shall be paid the amount of their traveling expenses from the funds of the Society.

The supervisors shall be chairmen of their respective boards of censors, and shall cause the examinations of applicants to be conducted in strict conformity to the plan adopted by the Board of Supervisors.

The censors of the several district societies shall meet semi-annually for the examination of applicants on the first Thursday in May and on the first Thursday in December.

A fee of three dollars shall be paid to the district secretary by an applicant for fellowship for each examination or re-examination by the censors. This shall be sent promptly to the treasurer of the general society for deposit in the funds of the Society. An applicant shall not be considered as possessing the requisite qualifications for fellowship unless approved by at least three censors. An applicant failing two examinations shall be disqualified from again applying for fellowship until three years have elapsed from the date of the last application.

AMENDMENT 10. Change Chapter V, Section 2, to read:

(a) An applicant for fellowship who is a graduate of a medical school or college recognized by the Council shall apply on a form furnished for the purpose to the secretary of the district in which he has legal residence not later than February 15 for the May censors' examination or September 15 for the December censors' examination. At this time the district secretary shall verify the applicant's diploma and shall deliver the application form to the secretary of the general society not later than February 20 or September 20 respectively. An applicant nonresident in Massachusetts shall apply to the secretary of the Suffolk District Medical Society and shall be examined by the censors thereof. Consideration of a late application shall be postponed until before the next succeeding examination. The names of all such applicants, their addresses, medical schools and colleges, dates of graduation and the names and addresses of the various district secretaries shall be published in a list in the first number of the *New England Journal of Medicine* on or after March 5 or October 5. Confidential communications regarding the qualifications of applicants for fellowship shall be requested of the fellows of the Society to be sent to the appropriate district secretary not later than March 15 or October 15.

(b) An applicant for fellowship who is a graduate of a foreign medical school or college or a domestic medical school or college not on the list recognized by the Council or of a medical school or college no longer in existence, and who has practiced for a minimum of five years, shall apply for fellowship in like manner with the following exceptions and additions:

At the time of application the applicant must submit the name and address of a fellow of the Society who has agreed to act as his sponsor. The sponsor's duty is to obtain from fellows of the Society who are acquainted with the applicant and his work, confidential written opinions regarding his qualifications

for fellowship to be mailed directly to the district secretary not later than March 15 or October 15. The list of these applicants published in the *New England Journal of Medicine* shall also include the names and addresses of the applicants' sponsors.

The president, secretary and supervising censor of the district society, sitting as a local board of membership, shall then gather such further information as is deemed necessary to determine whether an applicant is a capable and conscientious practitioner of medicine and possesses a good professional reputation among his colleagues. Every candidate must be personally interviewed by this board.

The district secretary shall deliver to the chairman of the Committee on Medical Education a complete confidential file of all applications including correspondence, and the written recommendations of the local board with supporting reasons for advocating the acceptance or refusal of each applicant not later than April 1 or November 1. The Committee on Medical Education shall then determine whether or not each candidate shall be approved for examination by the censors, and shall notify the district secretary and each applicant of its decision not later than April 20 or November 20.

AMENDMENT 11. Amend Chapter V, Section 3, to read:

District secretaries, who shall act as secretaries of their respective boards of censors, shall furnish applicants with forms adopted by the Board of Supervisors; they shall keep a complete record of all applicants for fellowship; they shall see that each applicant pays the examination fee; . . .

AMENDMENT 12. Add to Chapter VI, Section 1, the following:

He shall call at least one meeting of the Executive Committee of the Council between Council meetings, and may call more meetings if he so desires.

AMENDMENT 13. Change Chapter VI, Section 3, to read:

The Secretary may assign to an executive secretary any or all the duties now to be enumerated, except as specified below:

The Secretary shall attend all meetings of the Society and of the Council, and shall record their respective proceedings in separate record books; and this duty he may not assign.

He shall cause to be engrossed and shall sign the diplomas of new fellows if satisfied that they have met the requirements of Sections 1 and 2 of Chapter I, and shall issue all diplomas and certificates of fellowship. He shall notify individual fellows, in appropriate instances, of votes by the Council granting permission, as the case may be, to retire, to resign, to change district membership, to have dues remitted, or of votes depriving them of the privileges of fellowship; and these duties he may not assign.

He shall act *ex officio* as secretary of all boards of trial; and this duty he may not assign.

He shall have custody of the seal of the Society and of all books, papers, manuscripts, prints and paintings belonging to the Society, except such as are in charge of the Treasurer; and this duty he may not assign.

He shall act *ex officio* as secretary of the Board of Supervisors and of the Committee on Publications and the Committee on Ethics and Discipline, and shall keep the records of each in a separate volume. He shall have custody of all records as thus kept.

He shall issue notices of the meetings of the Council. One month before the annual meeting of the Society, he shall issue to every fellow a program which shall contain notification of the time and place of the annual meeting, notification of the stated meetings of the Council for the year and the meetings of the boards of censors, and information concerning the payment of assessments and the distribution of publications.

He shall keep a complete list of the fellows of the Society, with their addresses so far as known. He shall transfer fellows from one district to another under the terms of Chapter III Section 2, and shall report to the Society at its annual meeting the changes in membership of the Society during the year.

He shall conduct the official correspondence of the Society and shall notify officers, delegates and members of the committees of the Society of their appointments and of their duties.

Under the direction of the Committee on Publications he shall issue at such intervals as may be determined by the Council a directory of officers and fellows of the Society, which shall be furnished upon request to fellows who are not in arrears.

He shall perform such other duties as the Society or the Council may require.

#### AMENDMENT 14 Change Chapter VI, Section 5 to read

The Executive Secretary shall hold office at the pleasure of the Executive Committee of the Council.

He shall perform such duties as are assigned to him in Section 4 of this chapter and by the Executive Committee. In general he shall assist the officers of the Society and such standing and other committees as may request his services and the Society shall have the first call upon his services.

He shall attend all meetings of the Council and no request attend the meetings of the Executive Committee of the Council, but shall not vote in either.

The Executive Secretary need not be a physician.

#### AMENDMENT 15 Amend Chapter VII, Section 5, to read

The Committee on Medical Education shall consist of five fellows. It shall consider all matters relating to medical education which may be referred to it by the Council. It shall review the case of every applicant for fellowship who presents a diploma according to the provisions of Chapter V, Section 2(b). It shall have the power to approve for examination by the censors such an applicant and all decisions of the committee thereon shall be final. It shall revise the list of medical schools and colleges recognized by the Council annually for approval by the Council.

#### AMENDMENT 16 Amend the first paragraph of Chapter IV Section 1, to read

The Council shall consist of councilors chosen by the district societies and the president, ex-presidents, president elect, vice president, vice presidents *ex officio*, secretary and treasurer of the general society, secretaries of the district societies and the chairman of each standing committee.

#### AMENDMENT 17 Amend the first paragraph of Chapter IV Section 3 to read

The Council at its annual meeting on nomination by the Nominating Committee and/or from the floor shall elect by ballot officers of the Society as follows: president elect who shall serve as president elect until

the annual meeting of the Society next ensuing after his election and shall become president on his installation in the course of that meeting serving thereafter as president until the next following annual meeting and the installation of his successor a vice president, secretary and treasurer, all of whom shall assume the duties of office at the close of the annual meeting of the Society and shall hold office until their successors have been duly elected except only that at the annual meeting of the Council in 1941 there shall be nominated and elected a president to serve for that year.

In the absence of a president elect the Council at its next annual meeting shall upon nomination by the Nominating Committee and/or from the floor elect a president. Councilors only shall be eligible to the offices above named. Upon nomination by the Nominating Committee the Council shall elect by ballot a fellow to deliver an oration at the annual meeting of the Society the following year.

#### AMENDMENT 18 Change Chapter VI Section 3 to read

The President Elect shall assist the President in the performance of his duties in such a manner as the President may direct and in so doing shall be considered to represent the President.

#### AMENDMENT 19 Change Sections 3, 4 and 5 Chapter VI to Sections 4, 5 and 7 respectively

Dr Leroy E. Perkins moved that a vote of thanks be extended to the Committee of Arrangements for the very excellent program that had been presented, the motion was seconded and carried.

Dr Phippen then gave his report on the state of the Society.

It is my duty at this time to report on the state of your society. It is a pleasure to say that it continues to grow and prosper. Its activities are expanding. Its influence is beginning to be felt. A larger proportion of members are giving more thought to the affairs of the parent society. The attendance at Council meetings has been very gratifying and denotes I believe a more careful selection of councilors by the district societies. Only men who are willing and able to give freely of their time and thought should be elected to these important positions.

The total membership now numbers 5639 an increase of 97 in the past year.

The Society sustained a great loss during the year to the death of its very able secretary Dr. Alexander S. Begg. Dr. Begg was devoted to the interests of the Massachusetts Medical Society. He knew its history and its traditions. He probably knew more members intimately than any other member. Moreover he was a keen judge of men and knew who could be entrusted to do any particular job well. We miss him sadly but in so doing rejoice in his acquaintance and do honor to his service.

Our able and devoted treasurer reports again that our finances are as sound as the times will allow. He has continued his policy of placing funds of the Society in bonds and in most cases only in the best. One result of this is lower interest rate but with greater security of principal. At present the Society has a large amount of cash awaiting investment owing mainly to the receipt of 1941 dues. The Treasurer has not been able to invest

all in securities fit, in his opinion, for our funds. Almost all the Society's holdings of bonds are well above the cost prices. The Society, so far in 1941, has received from securities sold or from securities called for early payment a profit of several hundred dollars. No default in interest receivable has occurred this year, other than the issues already in default for several years. Collections of annual dues from resident fellows, to May 1, are greater than in 1940 for the same period. Nonresident dues received are also greater than in 1940. Expenses through April, 1941, have shown increases, but not to an unreasonable degree.

The Treasurer regrets that he feels obliged to carry such a large amount of cash awaiting investment. This idle cash should be earning income for the Society. The Treasurer is seeking, and occasionally finding, what he thinks is a proper medium for our funds.

A goodly number of fellows of the Society have been called to active duty with the United States Army and Navy. Some of these have asked to have their 1941 dues remitted.

Again I congratulate the Society on the wisdom and sagacity of its treasurer, and again I thank the Treasurer in the name of the Society for his conscientious and able service.

The standing committees have continued their efficient work.

It is a pleasure to note that the Committee on Ethics and Discipline has had rather less troublesome problems. We hope this is a good augury.

The Committee on Postgraduate Instruction conducted a very successful assembly for the third successive year. Again rain interfered, and it is planned to hold the Assembly earlier this year in the hope of better weather. The papers were excellent, and the question-and-answer period at luncheon was particularly worth while. The district courses have been continued, but the attendance at some might have been better.

The Committee on State and National Legislation has had a busy year. The major portion of its work is over, however, for with the exception of the annual-registration bill, the various premarital blood-test bills, the nurses' bill and some recently entered bills dealing largely with defense, the final reports are in.

Not every bill we favored was passed, nor was every bill we opposed turned down; but the important ones have gone our way, or at least have been put over for another two years. The Chiropractic Bill was beaten, and the Osteopathic Bill was withdrawn by the proposers, as was the bill to study the practice of surgery. The two bills to postpone and nullify the operation of the Approving Authority were given leave to withdraw.

Along with the Committee on Public Relations, and the Special Committee, the committee has spent a great deal of time and effort guiding our own enabling act through the Legislature. It was favorably reported by the Committee on Insurance and the Committee on Ways and Means, it passed the House, and yesterday it was passed by the Senate.

The hearings before the Committees were well attended, and I take this occasion to express the thanks of the Society to those members who gave their time to this duty.

I also thank the district chairmen for their splendid co-operation in the work of the Committee on State and National Legislation, and particularly the members of the Legislature, who gave the bill so much thought and so patiently listened to our arguments.

I am sure you all appreciate the time-consuming, ex-

acting work that Dr. Lanman and his committee have given to this problem. Much now remains to be done to set up the organization, and it cannot be done without your hearty co-operation.

The *Journal* has continued to improve in quality and in circulation. It is interesting to note that there has been an increase of over 1000 outside subscribers—that is, nonmembers of the Massachusetts Medical Society—in the last two years. Sixty-eight per cent of the papers presented to the editorial board were accepted, an increase of 6 per cent over the preceding year. The operating loss of \$20,438 is covered by your contributions to the *Journal*, which this year totaled \$20,500. I am sure we have every reason to be proud of the *Journal* and its very efficient editor.

I take this occasion to thank the editor for his willingness to undertake the additional duties of secretary *pro tempore*, a service that I am sure you all join with me in appreciating.

The Council, after thorough deliberation and debate, has recommended very comprehensive changes in the by-laws, which you have today approved. The setting up of the office of president-elect will, I believe, be of great benefit, in that it offers a year of apprenticeship, so to speak. The president will come into office with a far better knowledge of the Society and its component parts than is at present possible. The Executive Committee of the Council will prove to be a more and more useful piece of machinery as time goes on. Composed of one member from every district society it will be a truly representative body. The president has to decide many questions which arise between meetings of the Council that might better be referred to a representative body such as the Executive Committee will be. The by-laws now allow the appointment by the Executive Committee of an executive secretary, if and when the affairs of the Society seem to require such a full-time officer.

It seems to me that the time has come when the headquarters of the Society should assume a certain amount of dignity. It should offer hospitality to visitors and a wholesome welcome to our members. Here should be found daily lists of clinics and meetings. It should be modeled, perhaps, something like the Academy of Medicine in New York City, manned by a competent staff and open daily throughout the week. This might mean some structural rearrangement, but I believe it could be accomplished and in the doing add to the prestige of the Society. A full-time executive secretary would amplify this scheme. I commend it to your earnest consideration.

The changes in the by-laws relating to the admission of members deserve your careful reading. The requirements for admission to fellowship by an applicant who is a graduate of a foreign or substandard domestic medical school have been greatly strengthened. In the first place he must submit the name of a fellow who agrees to be his sponsor. In the second place a local board of membership is set up in each district consisting of the president, secretary and supervising censor, who must personally interview the applicant, weigh the evidence, form an opinion and report it to the Committee on Medical Education. This committee shall then decide whether the candidate shall be examined by the censors.

The machinery for the readmission of members has been somewhat simplified and at the same time strengthened. The time-consuming method of appointing special committees to consider applications for reinstatement has been abolished and the responsibility placed in the hands of a membership committee of each district society, whereas

the ultimate authority to recommend still resides in the Committee on Membership, and the Council, as heretofore, alone has power to readmit. The thanks of the Society are due to the members of the Committee on Medical Education for their very thorough work.

Your society has taken an active part in the preparedness program. Your members have responded loyally to serve on draft, advisory and appeal boards, giving generously of their time and strength without thought of compensation. The State Committee, headed by Dr. Fitz, through the district committees has helped to round up delinquent questionnaires. It has given such aid as it could to the Army-Corps surgeons and stands ready to render more when required. It co-operated with the three medical schools of Boston in sponsoring a meeting of the draft board and appeal board chairmen in an effort to persuade them that the education of medical students must not be interrupted until at least one year of internship shall have been completed and to urge them to defer medical students for this period. It is gratifying to note that the Selective Service Board has finally decreed that this is a proper procedure, provided each case is acted on individually, and that the student gives fair promise of becoming a reasonably good doctor.

Last June the Surgeon General of the Army proposed to the House of Delegates of the American Medical Association that they set up a committee to aid in the procurement of medical officers, recognizing that in the event of a national emergency it would be very necessary to conserve the medical profession and prevent the stripping of rural and isolated communities. This committee has been actively at work since then. Among other things we were asked to help in providing specialists for the various 1000 bed hospitals in the newly constructed camps. Lists of such available specialists were assembled and sent to the various Army-Corps surgeons within a short time. The General Staff, however, ordered that these specialists should be taken only from the Medical Reserve Officers Corps. The General Staff further decreed that no doctor should be newly commissioned in the Reserve Officers Corps above the rank of first lieutenant. It is therefore impossible for the Corps Area surgeons to obtain all the specialists they desire. It is hoped that some way may be found to utilize available and willing specialists and to give them a rank of captain or major, commensurate with the position and authority.

The Army estimates that its reserve corps will be exhausted by the middle of summer. It also estimates that it will need a yearly turnover of something like 9000 doctors. It seems wise at present that any unmarried doctor within the draft age should apply for a reserve officer's commission, rather than be drafted to an uncertain assignment. What lies ahead of us no one knows. We do know that the United States Army, Navy and Public Health Service need many doctors, and at the same time civilian needs must not be overlooked.

In closing I thank all the officers and committees for their untiring efforts and ready responses to my calls. Their loyalty and support have meant much to me in these somewhat trying two years.

It is difficult to find words to express to you, as members of this oldest medical society in America, my thanks for the high honor you have done me.

Dr. Phippen then introduced the orator, Dr. A. Warren Stearns, who delivered the Annual Discourse, "The Role of the Physician in a Competitive Society" (published in the May 22, 1941, issue of the *New England Journal of Medicine*).

Dr. Frank R. Ober, president for the ensuing year, was introduced and made a few remarks. The meeting was adjourned at 12 35 p.m.

Following the annual luncheon in the Swiss Room, a military symposium was held in the Sheraton Room, Dr. Dwight O'Hara presiding; the attendance was at least 500.

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There were twenty-two scientific and sixty-three technical exhibits, all of which were extremely well attended. The motion picture program, which covered both days, was so popular that sufficient seating capacity was not available.

The Ladies' Committee arranged an attractive program. On May 21, after a visit in the afternoon to the Isabella Stewart Gardner Museum, there was a dinner at the Roof Garden, Hotel Ritz-Carlton. A trip to the South Shore was made on May 22, including visits to the Dorothy Quincy House and Adams Mansion in Quincy and to the Cushing Homestead and Old Ship Church in Hingham, with luncheon at Hugo's in Scituate.

The annual golf tournament was held at the Commonwealth Country Club on May 21. Forty-two members participated, and the winners were as follows:

Low net (Burrage Bowl) — A. J. A. Campbell  
Second low net — H. E. Groden  
Third low net — L. F. Phylse  
Low gross — E. E. O'Neil  
Second low gross — Mirgan Sargent  
Third low gross — T. E. Dinan

The total registration was as follows.

Members and guest physicians	1525
Ladies	175
Total	1700

The lists of admissions and deaths are appended, together with the official lists of officers, standing and special committees, delegates, councilors, censors, section officers and officers of the district medical societies.

ROBERT N. NYE, *Secretary pro tempore*

## APPENDIX

ADMISSIONS RECORDED FROM MAY 22, 1940,  
TO MAY 22, 1941

YEAR OF ADMISSION	RESIDENCE	MEDICAL COUNCIL
1941	Ahrams, Herbert, Lowell	12
1940	Adams, Edward Everett, Roslindale	10
1941	*Adler, Alexandra, Boston	52
1941	Allan, Malcolm Stuart, Palmer	12
1940	Allen, Edward Carson, Brookline	12



1940	Anderson, Bertha Olive, Pittsfield	23	1940	*Gordon, Minerva, Attleboro	6
1941	Appleyard, Arthur Edward, Barre	12	1941	Goulston, Harold Francis, New Bedford	12
1940	Bachrach, Samuel, Worcester	12	1940	*Grace, James Joseph, Springfield	6
1941	Bayles, Theodore Bevier, Jamaica Plain	11	1940	Grassi, Michael Anthony, Haverhill	12
1941	Bell, George Olaf, Waban	11	1940	Gratwick, Mitchell, Andover	18
1941	*Bergmann, Louis, Brighton	52	1940	Greene, Daniel Crosby, Jr., Pittsfield	1
1941	*Berl, Adolf, Brighton	27	1940	*Grossman, Samuel, Roxbury	43
1941	*Beuthner, Bernard Hardy, Middleboro	48	1940	Hall, Volta Ross, Jr., Arlington Heights	42
1940	Bischoff, Arthur Jacob, Stoneham	28	1940	Hamilton, Thomas Stewart, Truro	13
1940	Bissell, George DeForest, Jr., Melrose	10	1940	Harrington, Philip Vincent, Worcester	11
1941	Bliss, Sheldon Pratt, East Braintree	12	1941	Haskell, Helen Stevens, Northampton	33
1940	Bowen, Donald Eyre, West Newton	12	1941	*Hauptmann, Alfred, Brighton	45
1940	Boyer, Norman Howard, Lexington	12	1941	Hayes, Donald Robert, Waltham	11
1941	*Brugsch, Heinrich Georg, Belmont	49	1940	*Heavey, Thomas J., Medway	6
1940	*Burger, Francis Joseph, Jr., Watertown	6	1941	Hertz, Saul, Brookline	11
1941	Burke, Arthur Edward, East Gardner	12	1941	*Hess, Leo, Brookline	52
1940	Burke, Edward William, Brighton	12	1940	Higgins, Raymond Francis, Worcester	9
1941	Butler, Henry Rutherford, Quincy	11	1940	*Hirsch, Oskar, Boston	52
1941	Butterfield, Paul Morgan, Harwich Center	1	1940	Hoerr, Stanley Obermann, Brookline	11
1941	Cahill, Francis Paul, Cambridge	11	1940	*Hollander, Alfred, Springfield	26
1940	*Camosas, Joao Jose Da Conceicao, Taunton	46	1940	Hollis, Charles Hilliard, Lawrence	12
1940	Campbell, Harry Lincoln, Medford	10	1940	Horne, Elwood Otho, Shrewsbury	12
1941	Carey, Edward Gerald, Boston	12	1940	Howard, Paul Malleville, Waverley	22
1941	Cary, Francis Frothingham, Springfield	11	1940	Huntington, Benjamin Lincoln, Boston	11
1940	Charron, Joseph Rosario, Turners Falls	37	1940	*Igersheimer, Josef, Boston	49
1940	Chase, Winnifred Pingree, West Medford	12	1941	Ingelfinger, Franz Joseph, Brighton	11
1940	Chesbro, Wallace Leo, Springfield	12	1940	Ishervood, Elizabeth Pynchon, Westfield	12
1940	Chisholm, Julian Ford, Jr., Boston	18	1941	*Izen, David Sidney, Medford	6
1941	Coco, Joseph Paul, Cheshire	43	1941	*Jessner, Lucie Johanna Ney, Georgetown	3
1940	Cole, Ralph Earle, Westford	12	1941	*Jossmann, Paul Bernhard, Brookline	54
1941	Collinson, Arthur William, Boston	12	1940	Jovell, John William, New Bedford	12
1941	Compson, James Enoch, Worcester	11	1941	*Kahn, Trude, Springfield	26
1941	Conlin, John Francis, Chelsea	12	1940	*Kant, Otto, Shrewsbury	35
1940	Connolly, Richard Francis, Danvers	19	1940	Kasparian, Karl Der, Boston	12
1941	Cordray, David Price, Boston	22	1940	Koczera, Stanley Joseph, New Bedford	12
1940	Crehan, Paul Joseph, Woburn	7	1941	Kranichuck, John Michael, South Hadley Falls	12
1941	*Cunningham, Joseph Anthony, Marblehead	30	1941	Kubik, Charles Soucek, South Lincoln	15
1941	Dalrymple, Leolia Agnes, Boston	32	1940	*Kwalski, Joseph Vincent, Ware	6
1940	*de Aguiar, Alcinda Pereira, Wrentham	55	1940	Lake, Fredric David, Springfield	11
1940	Dee, John Edwin, Worcester	11	1941	Lamphier, James Andre, Newton	12
1940	Deming, Julia, Boston	44	1941	Lane, Virginia Elizabeth, East Northfield	44
1940	Denhoff, Eric, Boston	7	1940	Larson, Carroll Bernard, Brookline	61
1941	Denton, Joseph Howard, Jr., Falmouth	24	1941	Lawrence, Knowles Birkinshaw, Brookline	1
1941	*Deutsch, Helene, Cambridge	52	1940	Lendgren, Carl Victor, Foxboro	10
1941	Dick, Vernon Shelton, Waban	38	1941	*Lepehne, Georg, Brookline	3
1941	Dieuaide, Francis Raymond, Boston	18	1940	Lepore, John James, Marlboro	19
1941	Dingle, John Holmes, Boston	11	1941	*Levinger, Max D., Fitchburg	31
1940	Dixey, Grant Milton, Marblehead	10	1940	Lewis, Elizabeth Katherine, Groton	12
1941	Doyle, Bernard Joseph, Easthampton	12	1940	Lewis, F. Woodward, Groton	12
1940	Dutton, David Parkhurst, Stoneham	11	1940	Lichter, Gerald Israel, Boston	14
1940	Edsall, Geoffrey, Cambridge	11	1941	Lowell, Francis Cabot, Cambridge	11
1940	*Elsberg, Albert, Brookline	49	1941	*Lowenthal, Frederick, Brookline	26
1941	Evans, James Ambrose, Waban	11	1940	*Lowenthal, Karl, Brighton	30
1941	*Faillace, Fedele Michele, Brookline	56	1941	*Lowenthal, Theresa Ulla, Brighton	49
1940	Farrington, Robert F., Boston	11	1941	Lewis, Samuel, Brookline	11
1940	Fell, Ernest Millward, Boston	12	1941	*Luisada, Aldo Augusto, Brookline	17
1941	*Fischmann, Joseph, Brighton	49	1940	MacDonald, Wilfred Daniel, Worcester	12
1941	Fisk, Evelyn Bernice, West Newton	7	1941	Marcus, Phillip Stephen, Boston	2
1940	*Fleischner, Felix George, Greenfield	52	1941	*Marnell, Thomas Frank, Great Barrington	8
1940	*Fleury, Edgar Joseph, Holyoke	6	1941	*Martin, Donald Alton, Waltham	5
1940	Foster, Frank Pray, Newton	9	1941	*Marx, Martin Simon, Brockton	31
1940	Friend, Dale Gilbert, Boston	11	1940	*Mastrangelo, Louis, Watertown	6
1940	Garber, Israel Enoch, Pittsfield	10	1941	*Mathews, Molyneaux Paul, Brockton	6
1941	Gardner, George Edward, Belmont	11	1941	*Mautner, Hans, Waltham	52
1940	Girouard, Fernand L., Attleboro	12	1941	McDaniel, Lewis Tillman, Boston	11
1940	Gladstone, Robert Warren, Pittsfield	7	1941	McDermott, Leo James, Boston	11
1941	Goehring, Harrison Dilwyn, Newton Upper Falls	47	1941	McDonald, Eugene Joseph, Boston	12
1941	*Goldstein, Kurt, Boston	48	1941	McFadden, James Marshall, Jr., Jamaica Plain	36
1941	*Goldstein, Walter, Brockton	49	1940	McGee, Charles Joseph, Brockton	11
			1940	*McSweeney, Timothy Hubert, Wilbraham	6



30.	University of Freiburg	48.	University of Breslau
31.	University of Munich	49.	University of Berlin
32.	University of Toronto Faculty of Medicine	50.	University of Frankfurt
33.	Cornell University Medical College	51.	New York University College of Medicine
34.	University of Nebraska College of Medicine	52.	University of Vienna
35.	University of Göttingen	53.	University of Strassburg
36.	Indiana University School of Medicine	54.	University of Geneva
37.	Laval University Faculty of Medicine	55.	Oporto University, Portugal
38.	University of Michigan Medical School	56.	University of Rome
39.	Friedrich-Alexanders University	57.	Northwestern University Medical School
40.	Kansas City University of Physicians and Surgeons	58.	Tulane University of Louisiana School of Medicine
41.	Emory University School of Medicine	59.	Jefferson Medical College
42.	Western Reserve University School of Medicine	60.	University of Minnesota Medical School
43.	University of Virginia Department of Medicine	61.	State University of Iowa College of Medicine
44.	Woman's Medical College of Pennsylvania	62.	University of Praguc
45.	University of Heidelberg	63.	University of Hamburg
46.	Lisbon University Faculty of Medicine	64.	University of Bern
47.	University of Pittsburgh School of Medicine		

## DEATHS REPORTED FROM MAY 22, 1940 TO MAY 22, 1941

ADMITTED	NAME	PLACE OF DEATH	DATE OF DEATH	AGE
1907	Andrews, Frederick Francis	Revere	November 7, 1940	68
1920	Begg, Alexander Swanson	West Roxbury	September 26, 1940	59
1875	†Benner, Burnham Roswell	Lowell	May 29, 1940	93
1904	Binford, Ferdinand Augustus	Hyannis	September 1, 1940	67
1912	†Blodgett, Stephen Haskell	South Lincoln	September 3, 1940	76
1933	Booth, Ernest Lazarus	East Boston	March 24, 1941	57
1887	†Bowen, John Templeton	Boston	December 3, 1940	83
1899	Briggs, Lloyd Vernon	Tucson, Arizona	February 28, 1941	78
1897	Carleton, Ralph	Springfield	October 26, 1940	70
1940	Chippendale, Francis David John	Fall River	November 19, 1940	28
1886	Clark, Joseph Payson	Boston	July 21, 1940	80
1926	Cleaves, Edwin Nelson	Boston	February 24, 1941	51
1895	Codman, Ernest Amory	Ponkapoag	November 23, 1940	71
1929	Copeland, Stanley Earle	Worcester	May 13, 1941	39
1912	Cotter, Timothy Francis	Haverhill	July 3, 1940	58
1933	Cox, Clyde Edward	Worcester	November 10, 1940	35
1920	Crawford, Joseph Warrington	North Adams	November 7, 1940	68
1903 } 1920 }	Crofts, Nicholas Matthew	North Adams	September 17, 1940	75
1904	Dailey, Edward Joseph	Somerville	December 10, 1940	61
1908	Darling, Arthur Edwin	Boston	June 19, 1940	62
1899	Davis, Charles Henry	South Hamilton	January 14, 1941	67
1907	†Davis, Frank Albert	Washington, D. C.	October 7, 1940	74
1934	Decker, John Joseph	Sioux City, Iowa	December 18, 1940	36
1886	†Dewey, Charles Gipson	Dorchester	April 18, 1941	81
1900	Elliot, Henry Libbey	Thomaston, Maine	June 27, 1940	66
1917	Emerson, Frederick Lincoln	Boston	November 10, 1940	78
1896 } 1919 }	†Enebuske, Claës Julius	Lund, Sweden	July 4, 1940	85
1929	Ferrini, Peter	Laconia, New Hampshire	August 5, 1940	39
1933	Fitzpatrick, Francis Joseph	Somerville	January 2, 1941	59
1891	†Francis, Carleton Shurtleff	Kerrville, Texas	March 8, 1941	75
1890	†Goodman, Samuel	Boston	May 28, 1940	75
1901	Greene, Daniel Crosby	Newton	April 4, 1941	68
1906	†Halsall, Mary Elizabeth	Winthrop	August 1, 1940	75
1908	Harmer, Torr Wagner	Winchester	October 2, 1940	59
1898	Harvey, William Wirt	Boston	November 10, 1940	74
1914	Hayes, William Francis	Beverly	April 4, 1940	58
1885	Henry, John Goodrich	Winchendon	January 18, 1941	83
1897	Hewitt, Clarence Elbert	Springfield	December 18, 1940	78
1904	Hill, George Jackson	Boston	October 29, 1940	61
1890	†Hitchcock, Henry Russell	Plymouth	November 23, 1940	79
1919	Hooper, George Henry	Belmont	July 24, 1940	48
1915	†Hoyt, Edward Malcolm	Georgetown	March 28, 1941	83
1894	†Hubbard, Osmon Huntley	Gilsum, New Hampshire	January 5, 1941	79
1891	Hutchings, Joseph Henry	Woburn	January 12, 1941	77
1884	Jackson, Henry	Chestnut Hill	October 4, 1940	82

1891 } 1920 }	Jenkins, Thomas Lincoln	Topsfield	July 29, 1940	74
1932	Kramer, Florence	Miami, Florida	January 15, 1941	56
1899	†Latham, Benoni Mowry	Taunton	July 24, 1940	67
1894	Lovell, David Bigelow	Worcester	September 18, 1940	75
1933	Magee, Edward Joseph	Danvers	January 20, 1941	77
1913	Mason, Gilbert McClellan	Dorchester	March 17, 1941	69
1928	Matzek, Neil Claytor	Bilmore	May 13, 1941	45
1890	†McCarthy, Thomas Horatio	Brockton	April 11, 1941	77
1897	†Mead, Frederick Ammi	Chicopee	November 5, 1940	71
1906	†Mellen, Eleanor Way Allen	Newton Highlands	April 19, 1941	72
1905	Mellus, Edward	Newton	December 7, 1940	68
1907	Morao, Charles Leo	Brighton	November 5, 1940	61
1933	Muir, Laura Helen	Roslindale	August 19, 1940	58
1916	Muldoon, Mary Theresa	Lexington	July 18, 1940	46
1914	Murphy, Edward Frederick	Jamaica Plain	January 15, 1941	64
1905	Murphy, Frederick Paul	Lowell	April 26, 1941	60
1905	†Murphy, Thomas William	Lawrence	November 2, 1940	70
1934	Murray, Michael Farley, Jr	Cambridge	April 21, 1941	36
1920	Nowell, Howard Wilbert	Brookline	October 28, 1940	68
1914	O'Rourke, Edward James	Cambridge	November 20, 1940	54
1894	Ott, George John	Boston	March 29, 1941	73
1913	Packard, Loring Bridford	Brockton	April 12, 1941	64
1898	Pige, Joseph Gregory Elias	Southbridge	December 28, 1940	69
1914	Parker, Raymond Brewer	Winthrop	October 19, 1940	55
1891	Pease, Edward Allen	Pasadena, California	June 19, 1940	75
1909	Pillsbury, Fritzon Farnsworth	Saco, Maine	June 18, 1940	55
1873 } 1877 }	†Porter, Francis Edward	Auburndale	October 11, 1940	96
1922	Renaud, Ulric Joseph	Brockton	August 12, 1940	43
1891	†Richardson, Aona Gove	Roslindale	February 1, 1941	80
1913	†Richardson, Oscar	Roslindale	August 28, 1940	80
1890	Rogers, Albert Edward	Boston	August 8, 1940	72
1893	†Rogers, Frank Alvin	Roxbury	November 15, 1940	95
1919	Ruggles, Edwin Pakeoham	Dorchester	June 19, 1940	77
1895	St Clair, Austro Emery	Frammingham	August 7, 1940	75
1891	Sanborn, Perley Lewis	Marlborough	February 3, 1941	90
1894	Sears, George Gray	Boston	May 28, 1940	81
1895	†Shattuck, Albert Milo	Worcester	May 26, 1940	69
1902 } 1912 }	Shea, Peter Owen	Worcester	March 9, 1941	70
1914	Simmons, Lt Col Ralph Hayward	Washington, D C	March 13, 1941	52
1895	Stanley, Josiah Murch	Northboro	June 4, 1940	80
1928	Sutherland, John Prestoo	Boston	February 21, 1941	87
1908	Swan, Lawrence Clarke	Beverly	October 2, 1940	59
1892	†Swan, Roscoe Wesley	Worcester	October 13, 1940	80
1895	Sweet, Frederick Benoni	Springfield	May 10, 1941	70
1897	Thorndike, Augustus	Bar Harbor, Maine	August 23, 1940	77
1938	Villone, Anthony Joseph	Quincy	October 6, 1940	49
1917	Vivian, William James	Northport, New York	June 10, 1940	56
1915	Walker, Melvin Harvey, Jr	Pittsfield	November 21, 1940	54
1913	Walsh, Edmund Francis	Nahant	August 20, 1940	56
1880	†Walton, George Lincoln	Boston	January 17, 1941	87
1905	Warren, Franklin	" "	February 11, 1941	69
1890	Weeks, Joshua	" "	January 12, 1941	74
1923	Welles, Delbert Arthur	Fitchburg	May 1, 1941	76
1919	Wetherell, Bryant David	Boston	March 5, 1941	52
1900	Whoriskey, John Joseph	Cambridge	July 26, 1940	63
1916	Williams, Frederick Horace	Boston	December 6, 1940	67
1879 } 1897 }	†Woods, George Lyman	Knoxville, Tennessee	July 28, 1940	90
1901	Wormelle, Charles Burton	Allston	September 16, 1940	68
1909 } 1933 }	†Worthing, Frank Bertelle	Chatham	March 13, 1941	71

†Retired fellow

Total number of deaths of active fellows 80  
 Total number of deaths of retired fellows 24

Grand total

104

## OFFICERS FOR 1941-1942

ELECTED BY THE COUNCIL MAY 21-22, 1941

PRESIDENT: Frank R. Ober, Boston, 234 Marlboro Street.  
 PRESIDENT-ELECT: George L. Schadt, Springfield, 44 Chestnut Street.  
 VICE-PRESIDENT: Edward P. Bagg, Holyoke, 207 Elm Street.  
 SECRETARY: Michael A. Tighe, Lowell. Office, Boston, 8 Fenway.  
 TREASURER: Charles S. Butler, Boston, 257 Newbury Street.  
 ORATOR: William B. Castle, Boston, Boston City Hospital.

## STANDING COMMITTEES FOR 1941-1942

ELECTED BY THE COUNCIL, MAY 21-22, 1941

*Date of Appointment*

## PUBLICATIONS — Established 1825.

R. M. Smith	June 6, 1933 (appointed chairman May 21, 1941)
J. P. O'Hare	June 9, 1936
Conrad Wesselhoeft	June 2, 1937
W. B. Breed	February 7, 1940
Oliver Cope	May 21, 1941

## ARRANGEMENTS — Established 1849.

W. T. O'Halloran	June 2, 1937 (appointed chairman May 1, 1941)
J. A. Halsted	June 1, 1938
G. P. Sturgis	June 7, 1939
H. H. Faxon	May 21, 1940
G. M. Morrison	May 21, 1941

## ETHICS AND DISCIPLINE — Established 1871.

R. R. Stratton	June 9, 1936 (appointed chairman May 21, 1941)
W. J. Brickley	February 3, 1937
A. G. Rice	June 1, 1938
F. R. Jouett	May 21, 1940
A. R. Gardner	May 21, 1941

## MEDICAL EDUCATION — Established 1881.

J. P. Monks	June 7, 1939 (appointed chairman May 21, 1940)
A. W. Stearns	June 9, 1936
G. D. Henderson	June 1, 1938
L. S. McKittrick	May 21, 1940
R. T. Monroe	May 21, 1941

## STATE AND NATIONAL LEGISLATION — Established 1894.

H. C. Marble	October 2, 1940 (chairman)
D. L. Lionberger	June 4, 1935
B. F. Conley	June 2, 1937
C. A. Robinson	June 1, 1938
E. M. Chapman	June 7, 1939

## MEMBERSHIP — Established 1897.

G. C. Caner	June 17, 1930 (appointed chairman May 21, 1940)
J. E. Fish	June 17, 1930
H. F. Newton	June 9, 1931
P. H. Leavitt	June 1, 1938
A. W. Reggio	May 21, 1940

## PUBLIC HEALTH — Established 1912.

F. P. Denny	June 1, 1938 (appointed chairman June 7, 1939)
Gerald Hoeffel	June 17, 1930
S. C. Dalrymple	June 4, 1935
H. L. Lombard	June 4, 1935
H. F. Day	June 7, 1939

## MEDICAL DEFENSE — Established 1927.

A. W. Allen	June 7, 1927 (appointed chairman June 7, 1939)
E. D. Gardner	June 7, 1927
W. R. Morrison	June 9, 1936
Horatio Rogers	June 7, 1939
G. S. Reynolds	May 21, 1941

## PERMANENT HOME — Established 1932.

W. H. Robey	February 24, 1937 (chairman)
C. G. Mixter	June 8, 1932
J. M. Birnie	June 8, 1932
C. S. Butler	June 4, 1935
E. C. Miller	June 4, 1935

## FINANCIAL PLANNING AND BUDGET — Established 1938.

John Homans	June 2, 1938 (chairman)
E. L. Hunt	June 2, 1938
C. F. Wilinsky	June 2, 1938
E. J. O'Brien, Jr.	June 2, 1938
P. P. Johnson	October 4, 1939

## SPECIAL COMMITTEES

## CANCER — Established 1917.

Shields Warren, chairman; F. G. Balch, E. M. Daland, P. E. Truesdale, C. C. Simmons.

## REPRESENTATIVES TO THE MASSACHUSETTS CENTRAL HEALTH COUNCIL

Barnstable: W. D. Kinney\*  
 Berkshire: R. J. Carpenter\*  
 Hampden: G. D. Henderson\*  
 Norfolk: F. P. Denny\*  
 Suffolk: R. B. Osgood\*  
 Worcester: E. C. Miller\*

## PUBLIC EDUCATION (a subcommittee of the Committee on Public Health) — Established 1930.

F. P. Denny, chairman; Gerald Hoeffel, secretary; G. R. Minot, W. H. Robey, R. M. Smith, E. H. Place, C. C. Simmons, J. H. Pratt, H. W. Stevens, J. B. Ayer, H. P. Mosher, F. R. Ober, E. P. Joslin, J. D. Barney, H. L. Lombard.

## PUBLIC RELATIONS — Established 1931. (One member appointed yearly by each district medical society; the president of the Society is chairman.)

## BARNSTABLE DISTRICT MEDICAL SOCIETY

M. E. Champion, North Harwich.

## BERKSHIRE DISTRICT MEDICAL SOCIETY

P. J. Sullivan, Dalton, 471 Main Street.

## BRISTOL NORTH DISTRICT MEDICAL SOCIETY

J. H. Brewster, Attleboro, 178 South Main Street.

## BRISTOL SOUTH DISTRICT MEDICAL SOCIETY

A. J. Pothier, New Bedford, 720 County Street.

\*Interim appointment

## ISSEX NORTH DISTRICT MEDICAL SOCIETY

E S Bagnall, Groveland 281 Main Street (Secretary of committee)

## ISSEX SOUTH DISTRICT MEDICAL SOCIETY

I D Reynolds, Danvers, 48 High Street

## FRANKLIN DISTRICT MEDICAL SOCIETY

H G Stetson, Greenfield, 39 Federal Street

## HAMPSHIRE DISTRICT MEDICAL SOCIETY

P F Gear, Hallowell 188 Chestnut Street

## HAMPSHIRE DISTRICT MEDICAL SOCIETY

L N Durgin, Amherst 66 Amity Street

## MIDDLESEX EAST DISTRICT MEDICAL SOCIETY

J H Blaisdell, Winchester Office, Boston 45 Bay State Road

## MIDDLESEX NORTH DISTRICT MEDICAL SOCIETY

D J Ellison, Lowell, 8 Merrimack Street

## MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY

D C Dow, Cambridge, 1587 Massachusetts Avenue

## NORFOLK DISTRICT MEDICAL SOCIETY

N A Welch, West Roxbury Office, Boston, 520 Commonwealth Avenue.

## NORFOLK SOUTH DISTRICT MEDICAL SOCIETY

F A Bartlett, Wolliston, 308 Beale Street

## PLYMOUTH DISTRICT MEDICAL SOCIETY

C D McCinn, Brockton, 12 Cottage Street

## SUFFOLK DISTRICT MEDICAL SOCIETY

A A Hornor, Boston, 319 Longwood Avenue

## WORCESTER DISTRICT MEDICAL SOCIETY

C A Sparrow, Worcester, 73 Sagamore Road

## WORCESTER NORTH DISTRICT MEDICAL SOCIETY

J J Curley, Leominster, 82 Main Street

## POSTGRADUATE INSTRUCTION—Established 1932

Reginald Fitz, chairman\*, L E Parkins, secretary, F D Adams, Roy Morgan, J M Birnie, H L Higgins, J W O'Connor, C W Blackett, Jr, R B Osgood, C S Burwell, A W Stearns, W H Robey, R N Nye, H D Chadwick, C M Campbell, Lincoln Davis

## PHYSICAL THERAPY—Established 1935

F P Lowry, chairman, R B Osgood, G R Minot

## COMMITTEE TO CONSIDER EXPERT TESTIMONY—Established 1936

G L Schadt, chairman, David Cheever, J J Goodwin, F P McCarthy, H C Marble

## AUTOMOBILE INSURANCE CLAIMS—Established 1937

H C Marble, chairman, H M Landesman, secretary, P P Henson.

## GERIATRIC CARE—Established 1938

T D Jones, chairman, H E Gallup

## INDUSTRIAL HEALTH—Established 1939

W I Clark, chairman, L R Daniels, D L Lynch,\* H G Murray, T L Shipman

\*Interim organization

## ARMY MEDICAL LIBRARY AND MUSEUM—Established 1939

H R Viets, chairman, R B Osgood, Benjamin Spector

## COMMITTEE TO STUDY PRACTICE OF MEDICINE BY UNREGISTERED PRISONERS—Established 1939

Richard Dutton, chairman, B F Conley, E F Timmins

## TWENTY FIVE VOTING MEMBERS IN THE ASSOCIATED HOSPITAL SERVICE CORPORATION—Established 1939

B H Alton, E S Bagnall, G M Ballboni, W B Brice, I D Chapin, H F Day, J F Donaldson, A W Dudley, J M Fallon, J E Flynn, A R Gardner, H W Godfrey, D C Halbersleben, J A Hukted, J H Lambert, A A Levi, A E Parkhurst, Helen S Pittman, A G Rice, A T Ronan, F W Snow, G I Steele, R P Stetson, J I Tibbot, E L Young

## COMMITTEE TO STUDY PROPOSALS FOR BUDGETING MEDICAL CARE—Established 1940

J C McCann, chairman\*, E S Bagnall,\* J M Birnie, T H Lumin, Shields Warren

## TAX SUPPORTED MEDICAL CARE COMMITTEE—Established 1940

E S Bagnall, chairman, A L Duncombe, A A Hornor, E L Hunt, W J Pelletier

## COMMITTEE TO MEET WITH MASSACHUSETTS HOSPITAL ASSOCIATION—Established 1940

H M Clute, chairman, B H Alton, R B Cattell, E D Gardner, A E Parkhurst, F W Snow

## COMMITTEE ON MEDICAL PREPAREDNESS—Established 1940

Reginald Fitz, chairman

## COMMITTEE TO EXAMINE WPA RECORDS—Established 1940

G L Richardson, chairman, W E Browne, D J Ellison, J R Chaput, F P McCarthy

## MATERNAL WELFARE—Established 1941

J A Smith, chairman, Thomas Almy, R L DeNorwiche, M Louise Diez, C J Duncan, M F Eades, A F G Edgelow, Rachel L Hardwick, J W O'Connor, L E Phaneuf, G M Shipton, W R Sisson, R M Smith, R S Titus, R J Williams

## COMMITTEE TO STUDY THE PRACTICE OF MEDICINE—Established 1941

Dwight O'Hara, chairman, B H Alton, A E Parkhurst, D D Scannell, Conrad Wesselloeff

DELEGATES AND ALTERNATES TO THE HOUSE OF DELEGATES, AMERICAN MEDICAL ASSOCIATION FOR 1941-1942

## DELEGATES

## ALTERNATES

June 1, 1940 to June 1, 1942

D D Scannell	E S Bagnall, Groveland
Janvier Pluin	
Dwight O'Hara, Waltham	E L Hunt, Worcester
C E Mongan, Somerville	M A Tighe, Lowell
W G Pluppen, Salem	J I B Vail, Hyannis

*June 1, 1941 to June 1, 1943*

J. M. Birnie, Springfield      R. J. Carpenter, Pittsfield  
R. H. Miller, Boston          Cadis Phipps, Brookline

## EXECUTIVE COMMITTEE OF THE COUNCIL

### *Members Ex-Officiis*

PRESIDENT: Frank R. Ober, Boston, 234 Marlboro Street.  
PRESIDENT-ELECT: George L. Schadt, Springfield, 44 Chestnut Street.  
VICE-PRESIDENT: Edward P. Bagg, Holyoke, 207 Elm Street.  
SECRETARY: Michael A. Tighe, Lowell. Office, Boston, 8 Fenway.  
TREASURER: Charles S. Butler, Boston, 257 Newbury Street.

*Term Expires 1942*

ESSEX SOUTH: Loring Grimes, Swampscott, 84 Humphrey Street.  
HAMPSHIRE: Lawrence N. Durgin, Amherst, 66 Amity Street.  
MIDDLESEX SOUTH: Dwight O'Hara, Waltham. Office, Boston, 5 Bay State Road.  
NORFOLK SOUTH: Daniel B. Reardon, Quincy, 1186 Hancock Street.  
SUFFOLK: Augustus Thorndike, Jr., Boston, 319 Longwood Avenue.  
WORCESTER: Ralph S. Perkins, Worcester, 10 Hackfeld Road.

*Term Expires 1943*

BARNSTABLE: William D. Kinney, Osterville.  
BRISTOL NORTH: William H. Allen, Mansfield, 70 North Main Street.  
BRISTOL SOUTH: Edwin D. Gardner, New Bedford, 150 Cottage Street.  
ESSEX NORTH: Frank W. Snow, Newburyport, 24 Essex Street.  
MIDDLESEX EAST: Kenneth L. MacLachlan, Melrose, 1 Bellevue Avenue.  
PLYMOUTH: Peirce H. Leavitt, Brockton, 129 West Elm Street.

*Term Expires 1944*

BERKSHIRE: John J. Boland, Pittsfield, 334 North Street.  
FRANKLIN: Frederick J. Barnard, Greenfield, 479 Main Street.  
HAMPDEN: George L. Steele, Springfield, 20 Maple Street.  
MIDDLESEX NORTH: William M. Collins, Lowell, 174 Central Street.  
NORFOLK: Carl Bearse, Boston, 483 Beacon Street.  
WORCESTER NORTH: John J. Curley, Leominster, 82 Main Street.

## COUNCILORS FOR 1941-1942

ELECTED BY THE DISTRICT MEDICAL SOCIETIES AT THEIR ANNUAL MEETINGS, APRIL 15 TO MAY 15, 1941

### BARNSTABLE

O. S. Simpson, Centerville, Main St., V. P.  
M. E. Champion, North Harwich, A. M. N. C.  
D. E. Higgins, Cotuit, Main St., Sec.  
C. H. Keene, Chatham, Seaview St.  
W. D. Kinney, Osterville, E. C., M. N. C.

### BERKSHIRE

W. A. Millet, Pittsfield, 225 North St., V. P.  
J. J. Boland, Pittsfield, 334 North St., E. C.  
R. J. Carpenter, North Adams, 85 Main St.  
I. S. F. Dodd, Pittsfield, 34 Fenn St.  
H. J. Downey, Pittsfield, 184 North St.  
C. F. Fasce, Pittsfield, 311 North St., A. M. N. C.  
C. F. Kernan, Pittsfield, 184 North St.  
G. S. Reynolds, Pittsfield, 7 North St., Sec.  
P. J. Sullivan, Dalton, 471 Main St., M. N. C.

### BRISTOL NORTH

J. A. Reesc, Attleboro, 48 Bank St., V. P.  
W. H. Allen, Mansfield, 70 North Main St., E. C., M. N. C.  
J. H. Brewster, Attleboro, 178 South Main St.  
R. M. Chambers, Taunton, Taunton State Hospital.  
J. L. Murphy, Taunton, 23 Cedar St., A. M. N. C.  
W. H. Swift, Taunton, 141 High St., Sec.

### BRISTOL SOUTH

H. P. Sawyer, Fall River, 68 Bigelow St., V. P.  
G. W. Blood, Fall River, 82 New Boston Rd.  
R. B. Butler, Fall River, 278 North Main St., A. M. N. C.  
E. F. Cody, New Bedford, 105 South Sixth St., M. N. C.  
J. A. Fournier, Fall River, 11 Choate St.  
E. D. Gardner, New Bedford, 150 Cottage St., E. C.  
F. M. Howes, New Bedford, 135 Cottage St.  
D. R. Mills, Edgartown.  
H. E. Perry, New Bedford, 159 Cottage St.  
A. H. Sterns, New Bedford, 31 Seventh St., Sec.  
I. N. Tilden, Mattapoisett, Barstow St.  
C. C. Tripp, New Bedford, 416 County St.  
P. E. Truesdale, Fall River, 151 Rock St.

### ESSEX NORTH

C. W. Bullard, Newburyport, 194 High St., V. P.  
E. S. Bagnall, Groveland, 281 Main St., A. M. N. C.  
R. V. Baketel, Methuen, 7 Hampshire St.  
L. R. Chaput, Haverhill, 3 Washington Sq.  
E. H. Ganley, Methuen, 251 Broadway.  
H. R. Kurth, Lawrence, 477 Essex St., Sec.  
P. J. Look, Andover, 115 Main St.  
R. C. Norris, Methuen, 247 Broadway.  
G. L. Richardson, Haverhill, 94 Emerson St.  
A. F. Shea, Lawrence, 62 Bradford St.  
F. W. Snow, Newburyport, 24 Essex St., E. C., M. N. C.  
T. N. Stone, Haverhill, 3 Washington Sq.  
C. F. Warren, Amesbury, 1 School St.

### ESSEX SOUTH

Bernard Appel, Lynn, 281 Ocean St., V. P.  
H. A. Boyle, Middleton, Essex Sanatorium.  
C. P. Brown, Swampscott, 74 Humphrey St.  
Hanford Carvel, Gloucester, 1038 Washington St.  
C. L. Curtis, Salem, 101 Federal St., A. M. N. C.  
R. E. Foss, Peabody, 125 Main St.  
S. E. Golden, Beverly, 38 Ocean St.  
Loring Grimes, Swampscott, 84 Humphrey St., E. C., M. N. C.  
P. P. Johnson, Beverly, 1 Monument Sq.  
J. F. Jordan, Peabody, 76 Lynn St.  
B. B. Mansfield, Ipswich, 4 Green St.  
A. E. Parkhurst, Beverly, Monument Sq.  
O. S. Pettingill, Middleton, Essex Sanatorium.  
W. G. Phippen, Salem, 31 Chestnut St., Ex-Pres.

E D Reynolds, Danvers, 48 High St  
J R Shrugnessy, Salem, 24½ Winter St, Sec  
J W Trask, East Lynn, 90 Ocean St  
C F Twomey, East Lynn 60 Ocean St  
C A Worthen, Lynn, 19 Park St

## FRANKLIN

A H Wright, Northfield, 111 Mun St, V P  
F J Barnard, Greenfield, 479 Mun St, E C, M N C  
H L Craft, Ashfield, Sec  
A H Ellis, Greenfield, 58 Federal St  
W J Pelletier, Turners Falls, 171 Ave A, A M N C  
H G Stetson, Greenfield, 39 Federal St, Ex Pres

## HAMPTDEN

G B Corcoran, West Springfield, 84 Park St V P  
I H Allen, Holyoke, 16 Fairfield St  
T S Bacon, Springfield, 69 Maple St  
F P Bagg, Holyoke, 207 Elm St, Vice President  
W C Barnes, Springfield, 146 Chestnut St Sec  
J B Bigelow, Holyoke, 109 Suffolk St  
J M Birnie, Springfield, 146 Chestnut St, Ex Pres  
W A R Chapin, Springfield, 121 Chestnut St  
J L Chereskin, Springfield, 333 Bridge St  
J P Derby, Springfield, 20 Maple St  
A J Douglas, Westfield, 93 Elm St  
E C Dubois, Springfield, 174 Buckingham St  
P F Gerr, Holyoke, 188 Chestnut St  
Frederic Hagler, Springfield, 20 Maple St  
G D Henderson, Holyoke, 312 Maple St  
E A Knowlton, Holyoke, 207 Elm St, A M N C  
M W Pearson, Ware, 19 Pleasant St  
A G Rice, Springfield, 33 School St, M N C  
G I Schadt, Springfield, 44 Chestnut St, President  
Eleet  
G L Steele, Springfield, 20 Maple St, E C

## HAMPSHIRE

Mary P Snook, Chesterfield, V P  
A J Bonnevillie, Hatfield, 60 Main St  
W J Collins, Northampton, 136 Mun St, M N C  
L N Dargun, Amherst, 66 Amity St, E C, A M N C  
J R Hobbs, Williamsburg, Mun St, Sec  
L B Pond, Easthampton, 115 Main St

## MIDDLESEX EAST

J M Wilcox, Woburn, 6 Bennett St, V P  
J H Blaisdell, Winchester, Office Boston, 45 Bay State Rd, A M N C  
Richard Dutton, Wakefield 33 Avon St  
E M Halligan, Reiding, 37 Salem St  
J H Kerrigan, Stoneham, 481 Main St  
K L Macchelin, Melrose, 1 Bellevue Ave, Sec, E C  
G R Murphy, Melrose, 244 Main St  
R W Sheehy, Winchester, 21 Washington St  
R R Stratton, Melrose, 538 Lynn Fells Parkway, M N C, C

## MIDDLESEX NORTH

W H Sherman, Lowell, 9 Central St, V P  
M L Alling, Lowell, 9 Central St  
H R Coburn, Lowell, 202 Merrimack St  
W M Collins, Lowell, 174 Central St, E C, M N C  
R L Drapeau, Lowell, 310 Merrimack St, Sec  
D J Ellison, Lowell, 8 Merrimack St, A M N C  
A R Gardner, Lowell, 16 Shattuck St  
W F Ryan, Lowell, 219 Central St  
M A Tighe, Lowell, 9 Central St, Secretary

## MIDDLESEX SOUTH

H F Day, Cambridge, Office Boston, 412 Beacon St, V P  
C F Atwood, Arlington, 821 Massachusetts Ave  
E W Barron, Malden, Office Boston, 20 Ash St  
W B Bartlett, Concord, 28 Monument St  
Harris Biss, Everett, 351 Broadway  
S M Biddle, Cambridge, 206 Huron Ave  
E H Bigelow, Frammingham Center, 31 Pleasant St, Ex Pres  
G F H Bowers, Newton Highlands, 156 Woodward St  
R N Brown, Malden, 621 Main St  
R W Buck, Wabun, Office Boston, 5 Bay State Rd  
E J Butler, Cambridge, 25 Garden St  
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 F. P. McCarthy, Milton, Office Boston, 371 Commonwealth Ave.  
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 L. W. Pease, Weymouth, 135 Webb St.  
 D. B. Reardon, Quincy, 1186 Hancock St., E. C., A. M. N. C.  
 H. A. Robinson, Hingham, 205 North St.

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 Charles Hammond, Hanover, Washington St.  
 W. T. Hanson, State Farm.  
 P. B. Kelly, Plymouth, 27 Court St.  
 P. H. Leavitt, Brockton, 129 West Elm St., E. C., A. M. N. C.  
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 R. C. McLeod, Brockton, Goddard Hospital, Sec.  
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 H. A. Kelly, Winthrop, 200 Pleasant St.

T H Lanman, Boston, 300 Longwood Ave  
 R I Lee, Boston, 264 Beacon St  
 C C Lund, Boston, 319 Longwood Ave  
 H C Marble, Boston, 270 Commonwealth Ave. C  
 G R Minot, Boston, Boston City Hospital  
 W J Mixer, Boston, 319 Longwood Ave  
 J P Monks, Boston, 330 Dartmouth St, C  
 Donald Munro, Boston, 618 Harrison Ave  
 H L Musgrave, Revere 622 Birch St  
 R N Nye, Boston, 8 Fenway  
 F R Ober, Boston, 234 Marlboro St, President  
 J P O'Hare, Boston, 520 Commonwealth Ave  
 W T O'Halloran, Boston, 475 Commonwealth Ave, C  
 L E Parkins, Boston 12 Bay State Rd  
 L E Phaneuf, Boston, 270 Commonwealth Av  
 Helen S Pittman, Boston, 412 Beacon St  
 W H Robey, Boston, 202 Commonwealth Ave  
 Ex Pres, C  
 G C Shattuck, Boston, 25 Shattuck St  
 R M Smith, Boston, 66 Commonwealth Ave C  
 Augustus Thorndike, Jr, Boston 319 Longwood Ave  
 E C  
 E F Timmins, South Boston, 527 Broadway  
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 Shields Warren, Boston, 195 Pilgrim Rd  
 Conrad Wesselhoeft, Boston, 315 Marlboro St  
 C F Wilinsky, Boston, 330 Brookline Ave

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 E C  
 J C Austin, Spencer, 176 Main St  
 Gordon Berry, Worcester, 36 Pleasant St  
 W P Bowers, Clinton, 264 Chestnut St, Ex Pres  
 L R Bragg, Webster, 260 Main St  
 P H Cook, Worcester, 27 Elm St  
 W J Delahanty, Worcester, 5 Trumbull Sq  
 G A Dix, Worcester, 6 Ashland St  
 E B Emerson, Rutland, Rutland State Sanatorium  
 J M Fallon, Worcester, 390 Main St  
 L M Feltin, Worcester, 36 Pleasant St  
 J J Goodwin, Clinton, 199 Chestnut St  
 E L Hunt, Worcester, 28 Pleasant St  
 E R Leib, Worcester, 36 Pleasant St  
 W F Lych, Worcester 390 Main St, A M N C  
 A W Marsh, Worcester, 690 Main St  
 J C McCann, Worcester, 390 Main St  
 J M Melick, Worcester, 27 Elm St  
 J W O'Connor, Worcester, 36 Pleasant St  
 W C Seelye, Worcester, 390 Main St  
 C A Sparrow, Worcester, 21 West St  
 G C Tully, Worcester, 34 Elm St, Sec  
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 F H Washburn, Holden, Holden Clinic  
 R P Watkins, Worcester, 332 Mun St, M N C  
 S B Woodward, Worcester, 58 Pearl St, Ex Pres

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 E A Adams, Fitchburg 40 Oliver St, Sec  
 H D Bone, Gardner, 19 Pleasant St  
 J J Curley Leominster, 82 Main St E C  
 C B Gay, Fitchburg, 62 Day St A M N C  
 J C Hales Gardner, 66 Parker St  
 B P Sweeney, Leominster, 5 Gardner Place, M N C

The initials E C following the name of a counselor indicate that he is a member of the Executive Committee the initials M V C that he is a member of the Nominating Committee and the initials A M N C that

he is an alternate member of the Nominating Committee. I P that a member is a counselor by virtue of his office as president of a district society and so vice president of the general society. C that he is chairman of a grand jury committee. Sec that he is secretary of a district society and Ex Pres that he is a candidate for being a past president

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## BARNSTABLE

W D Kinney Osterville supervisor  
 J H Higgins Marston's Mills  
 J I B Vul, Hyannis  
 C F Harris Hyannis  
 J I Chute, Osterville

## BERKSHIRE

I S F Dodd, Pittsfield, supervisor  
 M S Eisner, Pittsfield  
 G M Shipton, Pittsfield  
 John Hughes Pittsfield  
 G S Wickham Lee

## BRISTOL NORTH

W H Allen Mansfield supervisor  
 W H Bennett Taunton  
 L E Butler, Taunton  
 C B Kingsbury, Taunton  
 H L Rich, Attleboro

## BRISTOL SOUTH

F M Howes New Bedford supervisor  
 W F MacKnight, Fall River  
 F A McCarthy, Fall River  
 C C Persons, New Bedford  
 Henry Wardle, Fall River

## ESSEX NORTH

R V Brackett, Methuen, supervisor  
 L C Peirce Newburyport  
 J G Miller, Lawrence  
 O P Mudge, Amesbury  
 H B Perkins, Haverhill

## ESSEX SOUTH

A E Parkhurst, Beverly, supervisor  
 S N Gardner, Salem  
 C A Wortheo, Lynn  
 J J Hickey, Peabody  
 I B Hull, Gloucester

## FRANKLIN

W J Pelleuer, Turoers Falls, supervisor  
 A C I each, Orange  
 H M Kemp, Greenfield  
 L R Dame, Greenfield  
 K H Rice South Deerfield

## HAMDEN

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 G F Dalton, Springfield  
 W J Dillon, Springfield  
 P M Morrarty, Chicopee

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 M E Cooney, Northampton  
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T. F. Corriden, Northampton.  
C. H. Wheeler, Williamsburg.

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N. P. Hersam, Stoneham.  
C. E. Montague, Wakefield.  
M. J. Quinn, Winchester.

#### MIDDLESEX NORTH

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H. M. Larrabee, Tewksbury.  
F. R. Brady, Lowell.  
C. J. Lapniewski, Lowell.  
R. C. Stewart, Lowell.

#### MIDDLESEX SOUTH

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H. Q. Gallupe, Waltham.  
C. W. Finnerty, West Somerville.  
J. E. Vance, Natick.  
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Marjorie Woodman, Jamaica Plain.  
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Hyman Morrison, Roxbury.  
C. E. Allard, Dorchester.

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T. B. Alexander, Scituate.  
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#### PLYMOUTH

W. T. Hanson, State Farm, supervisor.  
J. H. Dunn, Rockland.  
G. A. Buckley, Brockton.  
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Donald Munro, Boston, supervisor.  
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#### WORCESTER NORTH

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### VICE-PRESIDENTS OF THE MASSACHUSETTS MEDICAL SOCIETY (*Ex-Officiis*) FOR 1941-1942

#### PRESIDENTS OF DISTRICT MEDICAL SOCIETIES

(Arranged according to seniority of fellowship  
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NORFOLK SOUTH — W. L. Sargent, Quincy.  
MIDDLESEX SOUTH — H. F. Day, Cambridge.  
MIDDLESEX NORTH — W. H. Sherman, Lowell.  
BRISTOL NORTH — J. A. Reese, Attleboro.  
HAMPDEN — G. B. Corcoran, West Springfield.  
PLYMOUTH — G. A. Moore, Brockton.  
SUFFOLK — A. A. Hornor, Boston.  
NORFOLK — S. A. Robins, Roxbury.  
WORCESTER NORTH — H. C. Arey, Gardner.  
WORCESTER — R. S. Perkins, Worcester.  
ESSEX NORTH — C. W. Bullard, Newburyport.  
MIDDLESEX EAST — J. M. Wilcox, Woburn.  
BRISTOL SOUTH — H. P. Sawyer, Fall River.  
BERKSHIRE — W. A. Millet, Pittsfield.  
HAMPSHIRE — Mary P. Snook, Chesterfield.  
ESSEX SOUTH — Bernard Appel, Lynn.  
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BRISTOL NORTH — J. W. Cook, Mansfield.  
BRISTOL SOUTH — A. C. Lewis, Fall River.  
ESSEX NORTH — F. W. Anthony, Haverhill.  
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FRANKLIN — H. N. Howe, Greenfield.  
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HAMPSHIRE — E. H. Copeland, Northampton.  
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MIDDLESEX NORTH — J. F. Boyle, Lowell.  
MIDDLESEX SOUTH — E. P. Stickney, Arlington.  
NORFOLK — W. J. Walton, Dorchester.  
NORFOLK SOUTH — F. A. Bartlett, Wollaston.  
PLYMOUTH — J. A. Carriuolo, Brockton.  
SUFFOLK — J. R. Torbert, Boston.  
WORCESTER — W. P. Bowers, Clinton.  
WORCESTER NORTH — J. C. Hales, Gardner.

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(The street addresses may be obtained from the  
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Charles L. Short, Boston.

## SECTION OF SURGERY

Chairman, Grintley W Taylor, Boston, secretary,  
James C McCann, Worcester

## SECTION OF PEDIATRICS

Chairman, Philip H Sylvester, Boston, secretary, James  
Marvin Bly, Belmont and Brookline

## SECTION OF OBSTETRICS AND GYNECOLOGY

Chairman, M Fletcher Edes, Newtonville and Boston  
vice-chairman, Christopher J Duncan, Brookline,  
secretary, Raymond S Titus, Boston

## SECTION OF RADIOLOGY AND PHYSIOTHERAPY

Chairman, Joseph H Marks, Boston, secretary, Henry  
A Tadjell, Wrentham

## SECTION OF DERMATOLOGY AND SYPHILIGOLOGY

Chairman, Arthur M Greenwood, Boston, secretary,  
William J Macdonald, Boston

# OFFICERS OF THE DISTRICT MEDICAL SOCIETIES FOR 1941-1942

## ELECTED BY THE DISTRICT MEDICAL SOCIETIES AT THEIR ANNUAL MEETINGS IN 1941

(The street addresses may be obtained from the  
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## MEDICAL PROGRESS

### PHYSIOLOGY\*

HEBBEL E. HOFF, M.D.†

NEW HAVEN, CONNECTICUT

THE increasing threat of war has directed the attention of physicians to some of the immediate medical problems created by war. The background of many of these problems lies in the work done in peacetime, with entirely different objectives. With this in mind, I have devoted this year's report to a consideration of the physiologic background of certain questions of topical interest.

#### ANOXEMIA IN THE NERVOUS SYSTEM

The brain is unusually susceptible to deprivation of oxygen. In contrast to many other tissues such as muscle, the dominant respiratory process in the brain in vivo is the oxidation of glucose, so that even momentary lack of oxygen seriously interrupts its metabolic activity.<sup>1</sup> Complete interruption of cerebral circulation produces unconsciousness in six to eight seconds, and all electrical signs of activity in the brain are obliterated in twenty seconds.<sup>2</sup> An anemia of two to fifteen minutes gives rise to irreversible changes in the cortex and medulla, and temporary blindness may follow anoxemia for five minutes.<sup>3</sup> The centers in the brain stem regulating respiration and the cardiovascular system are much more resistant, and may show recovery after complete anemia for as long as thirty to fifty minutes. This difference in the vitality of respiratory and cardiovascular centers and the cortex probably accounts for the cases not infrequently seen in which patients recover from respiratory failure under anesthesia, or from carbon monoxide poisoning, but show signs of irreversible cortical damage.

The electrical activity of the brain may be used as an index of cortical anemia.<sup>4</sup> Usually, no changes are seen until the venous blood from the brain shows an oxygen content below 30 per cent saturation (normal, 60 per cent). Then the faster alpha waves begin to diminish in frequency and amplitude, after an occasional initial period of increased rate. There then appears an augmentation in frequency and amplitude of the slower delta waves, and if the anemia persists and deepens, these waves may entirely replace the alpha waves.<sup>5</sup>

Seizurelike discharges may occur.<sup>4, 5</sup> Finally, all waves disappear.

States in which there is a cerebral anemia result in a similar type of electroencephalogram, characterized by the predominance of delta waves. Among these are carbon monoxide poisoning, nitrous oxide anesthesia with insufficient oxygen,<sup>6</sup> a reduced blood carbon dioxide level, and increased intracranial pressure.<sup>4</sup> It appears that a low blood carbon dioxide level causes constriction of the cerebral arteries, which may be sufficient to produce anemia. Increased intracranial pressure, whether from tumor, trauma or hemorrhage, apparently produces no changes until the intracranial pressure approaches to within 40 mm. of mercury of the arterial blood pressure.<sup>7, 8</sup> Any increase from this point diminishes the cerebral circulation, and is followed by the characteristic signs of cerebral anoxemia.

Many authors have emphasized the close relation between the influence of anoxemia and hypoglycemia on the brain.<sup>1, 5</sup> The general symptoms as seen in the various so-called "shock" treatments of mental illnesses appear to be much the same, whether the shock is produced by low blood sugar or by anoxemia.<sup>4</sup> The electroencephalogram in hypoglycemia is also very similar to that in anoxemia.<sup>9-11</sup> Changes appear when the blood-sugar level (in the internal jugular veins) falls below 35 mg. per 100 cc., and consist in an early decrease in rate and amplitude of alpha waves, followed by an increase in amplitude and frequency of the delta waves.<sup>4</sup> When the dependence of the brain on glucose oxidation is recalled, it is understandable that deprivation of either glucose or oxygen should have similar effects.<sup>1</sup>

These studies have an obvious relation to the problems of aviation. As the altitude at which a plane flies increases, the partial pressure of oxygen decreases, and symptoms of anoxemia begin to appear. In general, most persons begin to show increased respiration at from 6000 to 10,000 feet. Symptoms of sleepiness, fatigue and headache usually appear at 10,000 to 12,000 feet. Impairment of cerebral functions may be evident at from 8000 to 15,000 feet, individual variations being considerable. Above 20,000 feet, there is a critical danger to life, and coma and convulsions may be

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expected. Naturally, physical exercise or small amounts of carbon monoxide in the inspired air may greatly lower the altitude at which alarming effects of anoxemia may occur.<sup>12</sup>

Recent studies of the reaction of respiratory mechanism to anoxemia are of interest because of their applicability to the problems of high altitude flying and of general anesthesia. Schmidt and Comroe have for some time called attention to the major importance of the carotid body in the mediation of respiratory changes in response to low oxygen, whereas the respiratory center itself responds to increased carbon dioxide. In passing, it should be remarked that one of these authors<sup>13</sup> has recently made series of minute injections into the respiratory center of acid solutions or of solutions containing sodium bicarbonate and carbon dioxide. Although the former solutions had very little influence on respiration, the latter produced a prompt increase in respiration. These experiments, therefore, add to the evidence that carbon dioxide, and not pH, is the adequate stimulus to the respiratory center.

Schmidt and Comroe<sup>12</sup> have offered evidence indicating that during anoxemia, or during deep narcosis, the respiratory center may be seriously impaired, so that the main drive to the respiration is afforded by the carotid body. When, in such circumstances, the oxygen content of the blood is suddenly increased, the carotid body also ceases to function, and the center is unable to carry out its function alone. Respiration then ceases, and may fail long enough to cause death. The authors suggest that this may be the mechanism of respiratory failure in operations in which oxygen is administered after a period of anoxemia, and warn that delay in starting to use oxygen may create an anoxemia that will make possible similar accidents when oxygen is finally taken.

The autonomic nervous system is also involved in the reactions to anoxemia. The increased rate of the heart, the elevation of the blood pressure and the contraction of the spleen appear early and become increasingly noticeable as the anoxemia progresses. They are seen in experimental animals and in man during exposure to low atmospheric pressures,<sup>14</sup> and point to stimulation of the sympathetic nervous system. There may often occur an abrupt crisis at a degree of anoxemia near that which may produce unconsciousness; the heart suddenly slows, auriculoventricular block appears, and the subject becomes pale and sweaty, and faints. These symptoms point to an overaction of the parasympathetic nervous system and, thus, may in part be prevented by atropine.

Such observations do not permit the conclusion that the type of autonomic response depends on

the intensity of the anoxemia. On the contrary, there is recent evidence that during asphyxia both sympathetic and parasympathetic systems are stimulated simultaneously (Hodes,<sup>15</sup> Feldman, Cortell and Gellhorn<sup>16</sup>). Hodes compared the response of normal and sympathectomized animals to exercise and found that, although the normal cat showed a marked acceleration, the sympathectomized cat showed a decrease in rate. He suggests that muscular exercise produces a local vasodilatation, which cannot be compensated for in the sympathectomized cat. The blood pressure then falls, cerebral circulation becomes inadequate, and cerebral anoxemia results. The cerebral anoxemia then stimulates the sympathetic and parasympathetic centers, and the sympathectomy permits the parasympathetic responses to develop without opposition. Feldman, Cortell and Gellhorn arrive at the same conclusion after demonstrating that, in the normal rat, anoxemia (breathing 7 per cent oxygen) causes a rise in blood sugar, whereas it causes a hypoglycemia in the adrenalectomized animal.

#### ANOXEMIA IN THE HEART

The electrocardiogram serves as the most valuable indication of the presence and extent of anoxemia in the heart. Analysis of the voluminous literature of clinical and experimental studies permits the following general conclusions to be drawn. When the oxygen content of arterial blood is reduced from 30 to 50 per cent by any of a variety of procedures, such as breathing air containing a reduced (12 per cent) oxygen content, a progressive diminution of the height of the T wave is noted. This reduction in the amplitude of the T wave, which may eventually progress to inversion, is seen in all three standard leads, and has been observed in man as well as experimental animals.<sup>17-19</sup> It has been observed in aviators during ascents to 5000 feet or over without supplementary oxygen.<sup>20</sup> There is occasionally some displacement of the RST segment, usually downward. When the oxygen content of the arterial blood is reduced below 50 per cent saturation, changes resembling those in myocardial infarction appear. These include further displacement of the RST segment (often elevation), and the development of the so called "coronary T wave." Increase in the amplitude of the Q wave is not a prominent feature. If the deficiency of oxygen is neither too severe nor too prolonged, no anatomic changes are found in the heart, although the electrocardiographic changes may persist for some time.<sup>21</sup> If the anoxemia is severer, and persists but does not entail complete deprivation of oxygen, some necrosis will occur, which is distributed in small

foci that are largely subendocardial. These will be replaced in time by diffuse fibrous tissue. Carbon monoxide poisoning in man has been found to produce just such a picture.<sup>22</sup> Various German authors have for some time pointed out that this type of necrosis occurs in coronary disease in which the vessels are narrowed enough to cause serious restriction of the coronary blood supply but still permit sufficient circulation to prevent massive infarction.

Master and his collaborators<sup>23</sup> have recently shown that this type of myocardial damage is associated with electrocardiographic changes indicative of the lesser degree of anoxemia described above, that is, reduction in amplitude of the T wave and slight depression of the RST segment, and propose the term "coronary insufficiency" to designate the condition. Their use of the term "coronary occlusion" for the state associated with massive myocardial infarction is perhaps less justified, especially in view of the most recent work of Blumgart, Schlesinger and Zoll,<sup>24</sup> who show that coronary occlusion may often occur without infarction.

#### THE NATURE OF THE ELECTROCARDIOGRAM

An adequate explanation for the changes seen in the electrocardiogram during anoxemia, and after massive infarction of the myocardium, is not yet available, largely because there is as yet no adequate explanation for the normal electrocardiogram. There has been, however, some recent work on this subject. Some time ago, Eppinger and Rothberger<sup>25</sup> made superficial lesions in the heart by various methods (for example, the injection of corrosives) and found that the surface injuries produced marked effects, whereas deep injuries, not affecting the surface, evoked only minor changes, if any. They concluded that the electrocardiogram was largely determined by the electrical activity of the surface of the heart. Recently the subject has been reinvestigated by other methods,<sup>26, 27</sup> which confirm the thesis of Eppinger and Rothberger.

One of the procedures<sup>27</sup> employed in the above studies consisted in treating the heart with isotonic solutions of potassium chloride, which were found to cause a local and reversible depolarization, similar to that produced by an injury. Areas of the surface of the ventricles thus treated failed to develop their normal action potentials, and the influence of this failure on the electrocardiogram could be determined. When the left ventricle was so treated, elevation of the RST segment appeared in all three conventional leads. The elevation increased as more and more of the surface was involved, until finally an upright monophasiclike

complex remained. Since this remained after maximal injury to the left ventricle, it was concluded that this complex represented the contribution of the right ventricle to the electrocardiogram, that is, the "dextrocardiogram." Injury to the right ventricle, on the contrary, produced a depression of the RST segment, which increased with extension of the area of injury until an inverted monophasiclike complex remained after maximal injury to the right ventricle. It appeared that this complex represented the contribution of the left ventricle to the electrocardiogram, that is, the "levocardigram." Other evidence proved that the dextrocardiogram and levocardigram were in fact derived from the right and left ventricles, respectively. When these curves were plotted, and summed algebraically, complexes closely resembling the normal QRST complexes were obtained. It was concluded that the normal electrocardiogram results from the algebraic summation of the dextrocardiogram and levocardigram.

Elevation of the RST segment may therefore be taken to indicate damage to the left ventricle, whereas depression denotes damage to the right ventricle. When the lesion is restricted to a single ventricle, the RST segment is displaced in the same direction in all three conventional leads, although the greatest displacement occurs in Lead 2. When, however, the injury involves areas of both the right and the left ventricle, Leads 1 and 3 show the maximal changes, and the displacement in one lead is opposite to that in the other. With lesions of the anterior surface of the right and left ventricles, elevation of RST occurs in Lead 1, together with depression in Lead 3. Posterior damage involving both ventricles causes depression of RST in Lead 1 and elevation in Lead 3.<sup>28</sup>

According to the theory outlined above, the T wave represents the algebraic summation of the terminal portions of the dextrocardiogram and levocardigram. Normally, the right ventricle is excited slightly before the left, producing the normal upright R wave. If the durations of the dextrocardiogram and levocardigram are equal, the latter would be expected to terminate after the former, since it begins somewhat later. The T wave would therefore be downward. If for any reason the dextrocardiogram were prolonged beyond the termination of the levocardigram, the T wave would be upright. Alterations in the relative durations of the dextrocardiogram and levocardigram were actually produced by local heating and cooling of the surface of the ventricles, and concomitant changes in the T wave of the electrocardiogram appeared that were in every detail consistent with these theoretical postulations.<sup>29</sup>

Studying the effects of coronary occlusion by means of direct and semidirect leads, Jachim and his associates<sup>30</sup> concluded that three different factors play a part in the production of the characteristic electrocardiographic patterns: disturbances in conduction, partial or complete depolarization in the area of greatest injury, with consequent failure of action potentials from this area, and delayed repolarization in tissue that although damaged remains excitable and produces an action potential when stimulated. In view of the similarity between the monophasic action current and the dextrocardiogram and levocardigram, it is more than likely that the postulates of these authors, which now apply to the electrogram derived from direct leads, may be extended to the electrocardiogram. The effects of anoxemia on the electrocardiogram should then find explanation in the influence of anoxemia on the dextrocardiogram or levocardigram.

#### SITOCK

Freeman et al.<sup>31</sup> believe that at least one factor in the causation of shock is overactivity of the sympathetic nervous system. It may be induced reflexly by the fall in blood pressure in hemorrhage, by the afferent nervous stimulation in trauma or by the cortical stimulation of concussion, and it serves the normal function of maintaining blood pressure. If, however, the stimulus that has produced the overactivity continues, the latter may progress to a pathological degree. Peripheral arterial constriction will then diminish blood flow in the periphery to such a degree that capillary anoxemia occurs. Capillary anoxemia will be followed by dilatation of the capillaries, by fluid loss from the blood stream, by increased blood concentration, and by a progressively falling blood pressure—in other words, by shock. Freeman has shown that shock may develop in animals following slow constant infusion of adrenalin into the blood stream, which is confirmed by Swingle et al.<sup>32</sup> Other authors doubt whether the adrenalin-sympathetic theory can be applied to all types of shock,<sup>33</sup> and present experiments which appear to show that the administration of adrenalin may be a helpful therapeutic measure in shock consequent to intestinal manipulation.<sup>34</sup>

It is more than likely that a variety of factors are involved in the genesis of the syndrome generally recognized as shock. One important example comes from renewed interest in the influence on shock of extracts of the adrenal cortex and allied substances. Swingle and his co-workers<sup>32</sup> have demonstrated that additional cortical extract will protect against shock caused by trauma, by intra-

peritoneal injections of glucose or by injections of adrenalin in adrenalectomized animals maintained on adequate amounts of cortical extract. These authors then studied the effectiveness in these situations of desoxycorticosterone, a synthetic substance that appears to have the same effect on mineral metabolism as cortical extract. Desoxycorticosterone, used prophylactically, protected against shock induced by trauma, by injection of glucose into the peritoneal cavity and by injection of adrenalin. It had no effect on the shock following intestinal stripping.

The efficacy of adrenocortical extracts in the prophylaxis of shock of course raises the question of the relation of potassium to the various symptoms of shock. There is evidence that serum potassium may rise in shock.<sup>35</sup> Study of the influence of slowly rising concentrations of potassium in normal dogs makes it questionable whether increases in potassium, below levels required to kill the animal, cause any of the symptoms of shock.<sup>36</sup> Whether potassium is responsible for death in shock cannot be stated. Recent studies have established criteria by which the question may be judged.<sup>37</sup> Serum potassium should be in the neighborhood of 15 milliequiv. per liter in the presence of a normal serum calcium. Much higher levels of potassium may be reached if the calcium is elevated.<sup>38</sup> Accompanying the rise in serum potassium, a characteristic sequence of electrocardiographic changes should appear in the following order: increase in the amplitude of the T wave, depression of the ST segment, disappearance of the P wave, intraventricular block and arrest, or terminal ventricular fibrillation. At present the only situation (apart from poisoning from injection of potassium) in which accumulation of potassium has been shown to have caused death is in experimental anuria.<sup>39</sup> In dogs in which anuria was induced by ligation of the ureters or by removal of the kidneys, potassium steadily accumulated in the blood, and when it reached toxic levels the animals died.

There is now at hand a report of fatal shock in man accompanied by anuria, following a bomb blast.<sup>40</sup> Potassium in the serum rose to about 11 milliequiv. per liter at death. The patient died suddenly, with a rapid fall in blood pressure and an irregular pulse. The evidence in this case is entirely consistent with death from potassium poisoning, but without serial electrocardiograms it is difficult to be certain that this was actually so. It appears that the combination of shock and anuria will be a not infrequent occurrence after bomb-blast injuries.<sup>41</sup>

The use of desoxycorticosterone to prevent shock



may not be entirely without dangers. Extreme muscular weakness resembling familial periodic paralysis has followed the repeated injection in dogs of large doses of the substance.<sup>42</sup> There are also reports<sup>43, 44</sup> of the development of cardiac failure in man when large doses are given, and the condition also occurs in dogs. The difficulty may be diagnosed by the low serum potassium, and potassium added by mouth seems to be a specific remedy. It is possible that under some conditions prolonged periods of low potassium may result in pathologic changes in the heart.<sup>45</sup>

### HISTAMINE

The subject of shock naturally recalls the question of the role of histamine. Two general reviews of the subject are most valuable, because in both an attempt is made to delimit the action of histamine, and to indicate the circumstances in which histamine is not the causative agent, as well as those in which it is implicated.<sup>46, 47</sup> Evidence for histamine release is perhaps best established in the "triple response" of the skin to injury (Lewis<sup>48</sup>). The resemblance of the triple response to the response of local anaphylaxis in the skin led Lewis to conclude that the antibody-antigen reaction in sensitized skin cells represented a special form of cell injury, which like other stimuli injurious to cells caused the release of a preformed histaminelike substance. This naturally led to the concept that many responses in anaphylaxis of other types are due to the liberation of histamine.

The release of histamine seems to be particularly well established in the physical and nervous allergies. The allergic reaction to cold or heat, which may be accompanied by extreme vasodilatation and a fall in blood pressure, also causes an increased secretion of highly acid gastric juice, which appears to be good evidence that histamine is involved. The urticarial reactions to nervous stimuli, exercise and temperature changes reported by Grant, Pearson and Comeau<sup>49</sup> are similar to reactions caused by histamine, and are presumably due to the release of histamine by cholinergic nerve fibers in the skin of susceptible persons. In anaphylactic shock in dogs and rabbits, release of histamine can account for the major symptoms. Evidence is available to implicate histamine as the active factor in other types of human allergy, but cannot be said to be conclusive. The demonstration that histamine can be liberated in the skin of susceptible persons by cholinergic nervous stimulation strengthens the possibility that asthma of nervous origin may arise from the release of histamine in the lungs by vagal stimulation.

Histamine may also play a part in the genesis

of the symptom complex arising from bacterial or other intoxication. The acute collapse following administration of the toxin of *Staphylococcus aureus* has been shown to result from the liberation of histamine.<sup>50</sup> Certain snake venoms also release histamine. In all these circumstances, other effects of the toxic agent may also appear, and may produce symptoms. Thus mercuric chloride liberates histamine,<sup>50</sup> but it also coagulates protein, both factors being important. On the whole, Feldberg<sup>46</sup> concludes that the acute effects of the intoxication are likely to be histamine effects, whereas the chronic effects are likely to be results of other actions of the intoxicating agent. It is of interest that a disease in horses can be shown to be due to the action of certain bacteria in the gastrointestinal tract, which decarboxylates the amino acid histidine to form histamine. Feldberg also points out that a diversity of quite unrelated factors may operate to liberate histamine, such as simple coagulation of cell protein, dissolution of lipoprotein combinations within the cell and mechanical injury. The substance therefore appears to be in some sort of union with the cellular protein.

Some reports have appeared of the successful use of histaminase to reduce the response of reactive cells to histamine. Other attempts have not been uniformly successful.<sup>40</sup>

### HIGH-PROTEIN DIET AS A PROTECTION AGAINST LIVER INJURY

The well-established practice of giving diets high in carbohydrate in conditions in which liver damage is a factor may require modification in view of recent experimental data, which indicate the even greater protection afforded by a diet high in protein.<sup>51</sup> Using chloroform as the toxic agent, Ravdin and his associates<sup>52</sup> found that starved animals were more susceptible, whereas animals fed high-protein diets were much more resistant than normal animals. Miller and Whipple<sup>53</sup> have confirmed these experiments in the dog. They find that a normal well-fed dog will tolerate an hour of chloroform anesthesia without showing liver necrosis. Normal dogs fasted for three days respond to the same treatment by the development of marked hyaline central necrosis of the liver, marked lowering of prothrombin and fibrinogen in the blood, increase in the bile pigment in the liver, increase in urinary nitrogen and clinical signs of intoxication. Some animals die in two to four days. Dogs with low serum protein (low-protein diets or plasmapheresis) can hardly tolerate fifteen to twenty minutes of anesthesia. A single large protein feeding will markedly increase the resist-

ance of these dogs to chloroform. The protective effect of certain irritant substances (sodium ricinoleate and colloidal carbon) may be due to the inflammatory reactions they evoke, and to the consequent increased protein catabolism.<sup>51</sup> There is some evidence that the sulfur-containing amino-acids have a role in the protective influence of protein.

A variety of other toxic agents affecting the liver are also shown to be influenced by a high protein diet. The most important is perhaps arsphenamine, which at times may cause liver damage when used therapeutically. Using admittedly high doses (0.03 gm. per kilogram) Messinger and Hawkins<sup>52</sup> found that both high-protein and high carbohydrate diets were protective, whereas fat diets were harmful. The toxic effects of selenium on the liver are also determined by the diet. A high-protein diet greatly reduces the liver damage produced by feeding selenium-containing wheat.<sup>53</sup> Lewis, Schultz, and Gortner,<sup>54</sup> who noted the increased resistance to selenium afforded by a diet containing 30 per cent casein rather than 6 per cent, found that methionine was protective, whereas cystine in equivalent dosage was not, although both are sulfur-containing aminoacids.

These studies emphasize two very practical points. First, they call attention, if this is still necessary, to the extreme hazards accompanying the use of chloroform as an anesthetic, especially if anoxemia is also a factor.<sup>55</sup> Secondly, they suggest that a high protein, high carbohydrate diet is required in any condition in which liver damage must be combated or prevented.

Associated with this problem are reports showing that a gum acacia, given for its osmotic pressure effect, accumulates in the liver and depresses certain liver functions.<sup>56-58</sup> Large quantities of the material may accumulate in the liver, and there act to diminish the production of plasma proteins, affecting most seriously the fibrinogen.<sup>51, 52</sup> Other liver-damaging substances enhance the depression of plasma proteins by acacia.<sup>59</sup> The depression of plasma proteins may last for several months after cessation of acacia injections, and the enlarged acacia-filled liver may persist for a long time. There is one report of its presence in the liver of a child to whom it was given six years previously.<sup>61</sup> Acacia does not appear to affect the production of bile salts or bile pigments, nor is it responsible for the alteration in blood and bile cholesterol.<sup>62</sup>

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 27271

#### PRESENTATION OF CASE

*First Admission* A forty-four-year-old Italian carpenter entered with the complaint of intermittent pain in the epigastrium of about three years' duration. Starting as a sensation of "knowing" in the epigastrium frequently associated with "burning" between the shoulder blades, it became progressively severer, developing into a sharp pain, which characteristically occurred thrice daily at 11 a.m., 5 p.m. and 11 p.m. and was readily relieved for a few hours by food or powders. Occasionally, the patient was awakened from sleep by an attack of pain, and on such occasions he usually felt nauseated. He rarely vomited, and the vomitus was never blood stained or black. He had never noted any black stools. During the first two years, his attacks had been interspersed between comparatively long periods of complete freedom from symptoms. In the last five months there had been no significant remission. He had lost about 25 pounds in the year before entry.

Nine months before admission the patient had visited the Out Patient Department, where a gastrointestinal series was reported as follows: "Examination of the esophagus shows no evidence of varices or herniation. The stomach is high in position and fills well. There is definite tenderness over the lesser curvature about 6 cm. from the hiatus, where there is an ulceration 1.5 cm. in width which extends 1 cm. outward from the body of the stomach. The antrum shows considerable spasm. The duodenal cap fills well and shows normal relief. The findings are those of a large gastric ulcer on the lesser curvature." A six meal bland diet was prescribed, with transient relief, but was not adhered to. An x-ray examination after seven months still showed the ulcer crater, although it seemed definitely shallower than on the first examination. Because of his unsatisfactory progress, hospitalization was advised.

The past history recorded an episode of "anemia" during service in the Italian army twenty years before, which was treated with a series of thirty-six daily gluteal injections. The patient's father was living and well at seventy-two, his mother

had died at fifty of unknown cause. One brother had attacks of "stomach trouble" associated with the vomiting of bright-red blood. His wife had had four children, all of whom were living and well.

Physical examination showed a sparse, muscular man lying comfortably flat in bed in no distress. The skin and mucous membranes showed no icterus or pallor. The nasal septum was deviated to the left. The teeth were carious, with some bleeding of the gums. The heart and lungs were normal, the blood pressure 100 systolic, 70 diastolic. Abdominal examination disclosed no tenderness, and no masses or organs could be felt. Rectal examination showed small hemorrhoidal varices. Reflexes were normal.

The temperature was normal, the pulse from 70 to 80, and the respirations from 15 to 20.

Laboratory examinations included a negative blood Hinton reaction. The red cell blood counts ranged from 4,700,000 to 4,900,000, the hemoglobins from 84 to 90 per cent (Tallqvist), and the white-cell counts from 7000 to 11,000. The differential count was 54 per cent polymorphonuclears, 34 per cent lymphocytes, 21 per cent monocytes and 2 per cent eosinophils. There were no abnormal cells, and the red cells showed no abnormalities. The urine varied from 1016 to 1030 in specific gravity and never showed albumin, sugar, diacetic acid or bile. The sediment was normal. Fifteen stools were brown in color and negative to the guaiac test. Two serum protein determinations showed 6.6 and 7.0 gm per 100 cc. The nonprotein nitrogen was 22 mg per 100 cc., and the blood chloride 101.6 milliequiv. per liter. A gastric analysis showed no free hydrochloric acid in the fasting contents, but 50 units after histamine.

The patient was placed on a regime of strict bed rest, a first stage ulcer diet, Amphogel and tincture of belladonna supplemented by subcutaneous atropine. His improvement was steady. Three x-ray examinations at intervals of approximately two weeks reported respectively: "The ulcer crater is definitely smaller and now measures 8 mm. in diameter", "The crater is much smaller and now measures approximately 2 to 3 mm. in diameter", "An ulcer crater is no longer visible." All reports, however, including the last, described shortening of the lesser curvature and spasm in the prepyloric area. Deformity of the duodenal cap was mentioned twice, but no spasm or evidence of active ulceration was noted. Two gastroscopic examinations were performed during the same period. The first described a typical benign ulcer 0.5 cm. in diameter, with slight granularity of the

surrounding mucosa. On the second examination no ulcer could be seen. The patient was discharged after nine weeks, apparently relieved.

*Second Admission* (nine months later). During the succeeding period, the patient was seen at irregular intervals in the gastrointestinal clinic of the Out Patient Department. Despite adherence to a six-meal diet, he had some discomfort almost every day, usually a sensation of burning between the shoulder blades rather than epigastric pain. X-ray examinations one and two months after discharge were inconclusive, mentioning spasm in the prepyloric area and questionable irregularity of the lesser curvature proximal to the area of spasm. The following month a gastroscopic examination demonstrated recurrence of the ulcer, with a crater 1 cm. in diameter and approximately 3 mm. in depth. The patient was advised to re-enter the hospital, but refused and disappeared for an interval of six months. On return he reported an episode two months before of increasing pain for several days followed by vomiting a large amount of bright-red blood and fainting. He was taken to another hospital, where he remained one week. In the two weeks before entry his pain had become severer and was no longer relieved by food or soda. An x-ray examination in the Out Patient Department was reported as follows: "Examination shows a normal esophagus and a high stomach, which lies in the transverse position and is beyond the reach of palpation." An ulcer could again be demonstrated on the lesser curvature almost as large as that noted at the first examination. The lesser curvature in the neighborhood of this ulcer appeared somewhat rigid and edematous. There was again spasticity of the prepyloric area, but this area opened up during the examination, filled and emptied well. The duodenal cap and remainder of the duodenum showed nothing abnormal. The mucosal folds in the stomach appeared somewhat hypertrophic. The diagnosis was "ulcer of the lesser curvature, which appears benign." Hospitalization was again advised, and the patient re-entered.

Physical examination was essentially unchanged, except that the mucous membranes showed pallor and the blood pressure was 140 systolic, 90 diastolic. His weight was 131 pounds, as compared with 126 on the first admission. The heart, lungs and abdomen were entirely normal. Examination of the blood showed a red-cell count of 4,900,000 with a hemoglobin of 10.5 gm., and a white-cell count of 8800. The differential count was 57 per cent polymorphonuclears, 24 per cent lymphocytes, 8 per cent monocytes, 10 per cent eosinophils and 1 per cent basophils. There were moderate achromia and variation in the size and

shape of the red cells. One of two urine examinations showed a + test for albumin. Two stool examinations were guaiac negative. A gastric analysis showed 18 units of free hydrochloric acid in the fasting contents and 41 units after histamine. The material was guaiac negative.

On the sixth hospital day a laparotomy was performed.

#### DIFFERENTIAL DIAGNOSIS

DR. HELEN PITTMAN: This seems to me like a very run-of-the-mill case.

I do not know anything about Italian medicine, but according to the little I know about French medicine everything is treated by injection, and I should assume that this patient had just what the record states, "an episode of anemia," and I am going to disregard it as having anything to do with the rest of the case.

The only interesting points in the laboratory findings are the 21 per cent monocytes, not borne out by a later count, and the absence of free acid in the fasting contents but the presence of acid after histamine. The two differential counts do not compare. One shows 21 per cent monocytes and 2 per cent eosinophils, and the next had 8 per cent monocytes and 10 per cent eosinophils. I shall assume that it is not very important.

Perhaps this would be a good time to see the x-ray films.

DR. TRACY B. MALLORY: I shall show lantern slides of the films. The lesion is so obvious that I can point it out without benefit of a roentgenologist. This was taken in March, 1939, showing a good-sized crater, situated just about the middle of the lesser curvature. The second slide shows the stomach a year and a month later, and the crater is absent. In the third picture, one year subsequently, it is back again and is of the same size as in the first examination.

DR. PITTMAN: I think that this is a perfectly classic story of recurrent gastric ulcer, which did very well in the hospital under supervision. When the patient returned home and was not under supervision it recurred, although he said he had adhered to his diet. He was operated on because of the danger of its being carcinomatous. I think he should have been operated on, and I should think no one would be able to tell what they were going to find.

The physical findings on the whole were quite normal. The patient developed no anemia; he had one period of frank bleeding, but no occult blood. His weight kept up; he had always had acid after histamine, and free acid was present at the second entry. I do not believe it is possible to

say whether he had a carcinoma or whether he had an ulcer. On the basis of the facts that he had not developed anemia, that he had not lost weight and that the general condition apparently was very good, I am going to guess that when they operated he still had a benign gastric ulcer.

DR. AUBREY O. HAMPTON: We could not tell any more than anyone else about this case. The diagnosis depends on the histology. The fact that the ulcer reduced in size—perhaps it did not quite disappear, but we thought it did—does not rule out carcinoma. Although some years ago I should have been fairly certain it was a benign ulcer, at present I am skeptical.

DR. EDWARD B. BENEDICT: I did three gastroscopies on this patient. At the first examination the lesion looked essentially benign. I thought he should be carefully followed. Two weeks later I did another gastroscopy and saw no ulcer, but pointed out the fact that it might be hiding behind the angulus. There is a blind spot where it is possible to miss an ulcer, and I still advised following him carefully by x-ray study and by gastroscopy. Two months later I saw him again and gastroscopied him, and the ulcer was there again. The recurrent ulcer still looked grossly benign, but I questioned the possibility of malignancy and advised him to enter the house. I think that from then on the history is misleading. I am quite sure he was completely lost track of for seven or eight months and not seen in the clinic. He refused to re-enter the hospital. When I next saw him this winter, x-ray study showed a definite recurrence, and the patient was advised to come in for resection.

DR. LELAND S. MCKITTRICK: Were you or any one else worried about the shortening of the lesser curvature described?

DR. HAMPTON: No. At one time that was thought to be commoner in benign than in malignant lesions, but I do not believe it is worth anything in the differential diagnosis. It means only spasm of the longitudinal muscles. It could occur in either type of lesion.

DR. HORATIO ROGERS: I should think the assumption would have been that this was malignant. With his age, with the change of symptoms and with the recurrence of the ulcer, I should have considered it malignant rather than benign. I am surprised that they assumed it the other way. What was the objection to operation at the first admission?

DR. BENEDICT: We advised hospitalization on the basis of potential malignancy when first seen in the Gastrointestinal Clinic, but the patient refused to come in.

DR. ROGERS: What is the prognosis of a man

of this age with an ulcer more than a centimeter in diameter in the stomach?

DR. HAMPTON: I do not know.

DR. MCKITTRICK: Do you not believe, if you want to be critical, you should go back nine months and ask why he had not been hospitalized when the diagnosis of gastric ulcer was first made?

DR. BENEDICT: Yes; nine months previously he was seen in our gastrointestinal clinic. Cancer should have been seriously considered, although the ulcer was not very large.

DR. MCKITTRICK: I do not care how large it is, Dr. Benedict. I think there is only one way to treat ulcers of the stomach and that is to treat them all in the hospital as soon as the diagnosis is made. The patient should become symptom free and the ulcer heal and remain healed, or else operation is indicated.

DR. BENEDICT: I agree, but the patient would not come in.

#### CLINICAL DIAGNOSIS

Peptic ulcer, benign

#### DR. PITTMAN'S DIAGNOSIS

Recurrent gastric ulcer.

#### ANATOMICAL DIAGNOSIS

Carcinoma of the stomach, with secondary peptic ulceration.

#### PATHOLOGICAL DISCUSSION

DR. MALLORY: This patient was operated on, and a lesion was found, which could not be differentiated from a benign ulcer. It was resected, and in gross it was impossible for the pathologist to say that it was anything other than a benign ulcer. When microscopic sections were made, it was apparent that there was something more. There was a deep area of peptic ulceration, lined by a typical fibrinoid layer, that had completely penetrated the muscularis and produced extensive scarring of the serosa. One small lymph node was drawn into the scar tissue, and sections through it showed a small focus, only 2 mm. in diameter, of colloid carcinoma, obviously a metastasis. Most of the ulcer appeared perfectly benign; no tumor could be found underneath the penetrating portion, but when its margins were examined it was quite clear that the mucosa, although of normal thickness, consisted entirely of malignant cells, a few of which were of the signet-ring type found in the lymph node. In most sections the tumor was entirely limited to the mucosa, but in one a submucosal lymphatic was found plugged with a thrombus of tumor cells.

Unquestionably in the interval during which the patient was observed this tumor changed from a carcinoma in situ to a frank invasive tumor, and metastasis developed. If the patient had been operated on while the cancer was still in situ, his chance of cure would have been better than 80 per cent, perhaps 100 per cent. It is doubtful if a tumor can metastasize until it begins to invade. With frank invasion and metastasis to a regional node, the chance of survival drops to about 30 per cent, even though it is still an early cancer.

### CASE 27272

#### PRESENTATION OF CASE

A twenty-two-year-old college girl entered the hospital complaining of epigastric pain and tenderness.

Five months before admission, at a time when the patient had been working very hard during and after school, she suddenly felt nauseated and vomited without apparent cause. The next day she began to have attacks of epigastric pain of unstated duration, which were severe enough to double her up. After several weeks of suffering, the patient consulted her physician, who made a diagnosis of peptic ulcer and prescribed hourly feedings and soda. This treatment gave only partial relief, and she found that warm milk was the most effective antidote. At no time had there been a change in bowel habits, melena, jaundice, vomiting or fever.

Two months before admission the patient married, and the attacks of epigastric pain grew worse, occurring in greatest severity about 1 a.m. At this time also the patient stated that she had had an attack of bronchitis, with fever, but no cough or hemoptysis. Six weeks before entry, she developed a sore mouth, and little blisters appeared on her gums and buccal mucous membranes. This condition grew worse until the patient was unable to eat and subsisted wholly on liquids for a few days. Her physician found that her gums were swollen and bled easily and prescribed a perborate mouth wash, orange juice, thiamine chloride and nicotinic acid, with the result that the condition cleared in five days. Three weeks before admission the epigastric pain became still severer and it was found that her temperature was 101°F.; the red-cell count was 3,200,000, the hemoglobin 50 per cent, and the white-cell count 16,000. Iron and liver extract were given, and a few days later the patient developed diarrhea, with six bowel movements daily, but no blood was noticed. Profuse night sweats appeared, and it was found that her temperature ranged from

99 to 102°F. She had missed her last two menstrual periods and had lost 12 pounds since the beginning of her illness.

The patient had had the usual childhood diseases, scarlet fever, and malaria at the age of eight years while in the tropics. The family history was irrelevant.

On examination the patient was well developed, but poorly nourished, pale and very ill. Examination of the heart, lungs and abdomen was negative except for slight epigastric tenderness; the blood pressure was 120 systolic, 48 diastolic. Pelvic examination was negative.

The temperature was 102°F., the pulse 90, and the respirations 30.

The urine was normal. The blood showed a red-cell count of 2,010,000 with a hemoglobin of 3 gm. (photoelectric-cell technic), and a white-cell count of 24,100 with 77 per cent polymorphonuclears. The sedimentation rate was 0.6 mm. per minute. The nonprotein nitrogen of the blood serum was 20 mg., and the protein 5.5 gm. per 100 cc. The blood Hinton reaction was negative. The stools were formed and black, and gave a ++++ guaiac test.

An x-ray film of the chest showed a primary complex in the right lower-lung field, with increased hilar calcification, but the lung fields were clear and the heart was not remarkable.

A gastrointestinal series showed a large mass occupying the greater portion of the body of the stomach, starting at the cardia and extending to an area approximately 4 cm. proximal to the pylorus. A large ulceration was present within the mass. The hourly follow-up films showed normal speed of transport through the small intestine. The loops of ileum were slightly dilated, and the barium within them had a somewhat pasty appearance.

One week after admission, gastroscopy was performed, and just inside the cardiac orifice about 2 or 3 cm. below the cardia was a smooth, rounded neoplasm projecting from the lesser curvature and involving the anterior and posterior walls, elevated above the surrounding mucosa 3 cm. or more and extending down at least to the angulus. In the central portion of the tumor there was an ulcerated, whitish sloughing area. In various portions there was definite hemorrhage, and old blood was present on the greater curvature. The angulus could not be identified, and the antrum and pylorus were not visible.

Three days later, peritoneoscopy was performed. A few ounces of clear fluid were aspirated from the peritoneal cavity, the liver appeared normal, the lesser curvature of the stomach lay under the

liver but was not adherent to it, and no tumor could be seen in the stomach. There was no evidence of metastatic disease throughout the peritoneum. A mass the size of an orange in the right side of the pelvis had the appearance of a benign ovarian cyst. No tumor cells were identified in the peritoneal fluid on pathological examination. Within the next two weeks the patient was given six 500-cc blood transfusions. Her temperature varied between 100 and 105°F. for a short while, but gradually fell to 99°F.; the white-cell count fell to 10,000, and the red-cell count rose to 3,900,000.

On the fourteenth hospital day an operation was performed.

### DIFFERENTIAL DIAGNOSIS

DR THOMAS J. ANGLE: May we see the x-ray films?

DR. AUBREY O. HAMPTON: Here is the large ulcer described in the stomach, a huge ulcerating lesion involving the whole of the lesser curvature except a small portion of the antrum. This is, I assume, the mass described in the right side of the pelvis. You see it outlined here by pressure on the small bowel. The chest was normal as described.

DR. ANGLE: What is the relation of the mass to the markings here?

DR. HAMPTON: The mucosal folds of the stomach are very thick all around it. The spleen and the liver are not enlarged.

DR. ANGLE: We are presented in this case with a large mass of clear cut and definite objective data that leave very little doubt concerning the basic nature of the underlying lesions. The problem is chiefly one of filling in the details and deciding on the precise nature of the neoplasm, rather than on the fundamental nature of the disease. That seems to have been settled for us by the gastroscopist, who reported a definite neoplasm in the stomach, described as being a large, round, smooth tumor mass with a grayish sloughing ulcerated center, so that I think we may start with the assumption that we are dealing with a neoplasm. For the sake of completing the differential diagnosis, one might mention briefly in passing the possibility of granulomatous disease. The case history and the x-ray findings and the finding of the gastroscopist, however, do not seem to be consistent with a diagnosis of tuberculosis or syphilis of the stomach, and in both these diseases, which are relatively rare, the typical picture is one of rather shallow serpiginous ulceration, and does not seem to fit this picture at all. Hence I think we can dismiss granulomatous disease.

If it is neoplasm, what kind is it—malignant or benign? If malignant, is it an epithelial tumor or a tumor of mesodermal origin? On a purely statistical basis, carcinoma of the stomach is, of course, by a wide margin the commonest neoplasm of the stomach, and the story presented in this case is entirely consistent with a diagnosis of carcinoma of the stomach. But there are certain features of the story that are atypical. If it is carcinoma, it would have to be of the polypoid type to be reconciled with the finding on gastroscopy. Against the diagnosis of carcinoma is the age of the patient. Carcinoma is very uncommon at the age of twenty-two, but it cannot be ruled out entirely on that basis. Also against the diagnosis of carcinoma are the relative absence of impairment of gastric motility and emptying and the abrupt onset of symptoms. The other tumors of the stomach that must be considered are the benign and malignant tumors of mesodermal origin. These are leiomyoma and its malignant variant, leiomyosarcoma, neurogenic sarcoma and lymphosarcoma. I wonder if I can find out more about the details of gastroscopic examination before going on with the differential diagnosis. Hemorrhagic areas are mentioned. Were they in the ulcerated portion or in the surrounding, smooth portion of the tumor?

DR. EDWARD B. BENEDICT: They were in the ulcerated portion.

DR. ANGLE: I think the least likely of the mesodermal tumors is lymphosarcoma. It is a relatively rare disease. It occurs in a form that originates in the stomach, and in a form with gastric involvement arising on the basis of a generalized lymphosarcomatosis. The picture presented on gastroscopy in this case, however, does not seem to be consistent with lymphosarcoma. We have here a large round, smooth, hard mass with an ulcerated center. Lymphosarcoma usually presents smaller masses than the one described here, although occasionally a large lobulated irregular polypoid tumor does occur. Some of the features of gastric lymphosarcoma are a soft consistence, with marked general vascularity and with scattered hemorrhagic areas in various parts of the tumor. I do not gather from the description of the findings on gastroscopy that they were consistent with this diagnosis.

Of the other mesodermal tumors that occur in the stomach, one stands out as the most likely diagnosis in this case, the malignant variant of leiomyoma, leiomyosarcoma. The history is entirely consistent with this diagnosis. There are certain features of the history that are difficult to reconcile, but in general it fits perfectly adequately.



Leiomyoma is the commonest benign tumor occurring in the stomach, and its malignant variant, although much less common than carcinoma, is not rare. It characteristically manifests itself by causing gastric distress or pain, and is associated frequently with epigastric tenderness of varying degree. A very common symptom is hemorrhage, causing either hematemesis or melena, or both. That is one of the features in this case which is difficult to reconcile with the picture presented by the patient on admission. We are told that the patient had a ++++ guaiac test on the stools at admission, and that the stools were dark, but beyond that there is no previous mention of either hematemesis or melena. Otherwise she presented a story that is entirely consistent with the clinical features presented usually by people with this disease: epigastric distress, starting abruptly in a patient previously in apparently good health, followed by increasing epigastric pain and clinical evidence in the patient's general decline, suggesting chronic blood loss in spite of the absence of clear-cut hematemesis or melena. The gastroscopic findings are entirely typical, presenting the usual picture, seen in leiomyoma or leiomyosarcoma of the stomach, of a round smooth mass occupying a large portion of the stomach wall, either anterior or posterior, with a central ulcerative area, frequently associated with bleeding points or hemorrhage from that area. Also characteristic of this disease is the relative absence of impairment of gastric function. There is very little, if any, impairment of gastric emptying, which we should hardly expect if the patient had a cancer of this size.

The next most likely possibility of the connective-tissue tumors that must be considered is neurogenic sarcoma. Neurogenic sarcoma can simulate leiomyoma and leiomyosarcoma in every detail, so that it is impossible to make a differential diagnosis between them on clinical grounds. The diagnosis is usually made by the pathologist.

There are certain features of this case that seem difficult to relate to the diagnosis that I have suggested, for example, the high fever and the very marked degree of anemia without a definite clinical history of blood loss by hematemesis or melena, but I believe that the answer to this apparent discrepancy is that this patient did have severe chronic blood loss in spite of the absence of such a history. I believe that the high fever and the anemia are the result of severe recurrent hemorrhage into the gastrointestinal tract. In support of that opinion is the finding that the patient responded very quickly and very readily to repeated transfusion,

with a rapid rise in red-cell count and a rapid fall in fever. There are minor symptoms, which I shall mention in passing, that I do not believe have any relation to the fundamental underlying disease. The stomatitis mentioned may have developed on the basis of vitamin deficiency, or may have been due to dehydration or faulty oral hygiene. The fact that it responded quickly to vitamin therapy suggests that it may have been due to vitamin deficiency. The amenorrhea may have been the result of chronic blood loss or possibly of pregnancy. The findings on peritoneoscopy I do not believe help us much, except to exclude a generalized malignant lesion. I am willing to accept the gastroscopist's opinion that the pelvic mass was an ovarian cyst. I believe this patient most probably had a leiomyosarcoma of the stomach, with hemorrhage into the gastrointestinal tract, with neurogenic sarcoma as the second choice, and benign cyst of the ovary.

DR. TRACY B. MALLORY: Dr. Hampton, do you want to express an opinion on the basis of the x-ray findings?

DR. HAMPTON: I think Dr. Anglem has the wrong impression from Dr. Benedict's story. I do not consider it fair to say that the tumor mass was round.

DR. BENEDICT: Do not forget that I won a dollar from the X-ray Department on this case.

DR. HAMPTON: I do not care if you did. I should say that the mass was relatively flat, with a rolled margin. The whole mass was not round, and the area of ulceration is very extensive and not very deep. That is more like lymphoma than leiomyosarcoma.

DR. BENEDICT: The edges of it certainly were rounded.

DR. HAMPTON: Yes; the edges were, but the mass was not.

DR. MALLORY: Have you anything further, Dr. Benedict?

DR. BENEDICT: No; I think Dr. Anglem is to be congratulated on his discussion. He has considered everything. I was unable to reach a positive diagnosis. I mentioned the most likely things, — carcinoma, leiomyosarcoma and lymphoma, — but was not willing to say which it was. We considered an open-tube gastroscopy with biopsy to establish a positive diagnosis, but decided that the patient should be explored anyway, so that we did not do it.

#### CLINICAL DIAGNOSES

Carcinoma of stomach?

## DR. ANGLE'S DIAGNOSES

Leiomyosarcoma of stomach?  
Neurogenic sarcoma?  
Ovarian cyst, benign.

## ANATOMICAL DIAGNOSIS

Fibrosarcoma of stomach

## PATHOLOGICAL DISCUSSION

DR. MALLORY: This patient was operated on, and a subtotal gastrectomy was done. A large tumor involved the lesser curvature almost from the cardia to the pylorus, and was extensively ulcerated. It had involved the entire thickness of the gastric wall and had reached the serosa. In gross it was no more possible to make an exact diagnosis than it was on clinical examination, but microscopic examination showed a rapidly growing spindle-cell sarcoma that looked more like fibrosarcoma than leiomyosarcoma. A few mitotic

figures and a great many tumor giant cells were present. However, no visible metastases were found. A great many enlarged nodes were present in the attached omentum, but they showed only inflammatory hyperplasia and one would not expect this tumor to go to the nodes in any case. I should think the picture on the whole bore out Dr. Hampton's contention as to the appearance of the tumor. The margin was round, but the tumor on the whole was rather flat, with a very extensive irregular area of shallow ulceration.

DR. HAMPTON: Is that more typical in gross of lymphoma than leiomyosarcoma?

DR. MALLORY: Yes. A diffuse spindle cell sarcoma of the stomach, with widespread invasion of the stomach wall, is quite uncommon. I remember one other very much like this, but ordinarily a spindle-cell tumor is quite well localized and has a tendency to be spherical.

DR. HAMPTON: The ulcer is usually much smaller and much deeper. I think that is the reason we lost a dollar. Next time we shall win it.

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## NURSING LEGISLATION

IN 1941, a bill to put control of nurses' registration and of nurses' training schools in a board of five nurses, with no representatives of the hospitals, physicians or public, was introduced by the Massachusetts Nurses Association. Hearings were held before the Committee on State Administration, and this committee has now reported out its own bill (House 2530), which increases the Board of Registration to four nurses and three physicians, including the secretary of the Board of Registration in Medicine *ex officio*. It provides for a paid nurse assistant to the secretary. This board is given control of registration.

The committee's bill also creates an approving authority to control all matters pertaining to training schools. This authority was composed as

follows: a nurse who is a faculty member of an approved school for nurses and a member of the Board of Registration; a nurse who is a faculty member of an approved school for attendants and a member of the Board of Registration; the secretary of the Board of Registration in Medicine; the commissioner of education; the commissioner of public health; a physician who is a superintendent or assistant superintendent of a hospital having an approved school for nurses or attendants; and a physician who is a member, with professorial rank, of the faculty of an approved medical school. The Massachusetts Hospital Association asked that the trustee of a charitable hospital be added, to represent the large interest of these institutions, and the Massachusetts Medical Society requested the addition of a practicing physician. With these additions, the bill has the approval of the Massachusetts Hospital Association and the Massachusetts Medical Society.

The bill also provides for the registration of attendants and approval of their schools.

The control of nursing schools, which are generally operated by hospitals, is thus placed in a committee composed of members representing the medical profession, the hospitals, the general public and nurses, and the bill also promotes the training of nursing attendants with recognized standing, to alleviate the shortage that is already occurring in the present emergency. This is as it should be. It is most important that the committee's recommendation be enacted into law.

## SIR D'ARCY POWER

THE death of Sir D'Arcy Power in England on May 18, 1941, at the age of eighty-five, brings to an end a useful career in both surgery and medical history. For nearly fifty years, D'Arcy Power was connected with St. Bartholomew's Hospital in London; he entered, as a student, in 1878 and left, as a consulting surgeon and one of the governors, in 1920. Few men have served a hospital for so long a period, and rarely has any-

\*Books, pamphlets and letters by Sir D'Arcy Power are now on exhibit in the rotunda of the Boston Medical Library.

one been more faithful to his parent institution. A few years after his retirement, he wrote *A Short History of St. Bartholomew's Hospital, 1123-1923* (1923), a fine example of what a hospital history should be. The chapters are brief and lively, and the illustrations, one in color showing the tomb of Rahere, founder of the hospital, form a unique feature of this admirable book.

The history of his own hospital, however, was not, by any means, the chief writing of D'Arcy Power. His bibliography goes back to 1881, when he published a little book, *Manual for the Physiological Laboratory*, with Vincent Harris, the demonstrator of physiology. At that time he was assistant demonstrator of the St. Bartholomew's Hospital Medical School and had joined the hospital staff in a subordinate position only a few years before.

As time went on, he continued to publish numerous works. One of his early books was *Surgical Diseases of Children* (1895), and in 1908 he edited *A System of Syphilis*, in six volumes, containing, among other chapters, an outstanding "Introduction" by Jonathan Hutchinson and a "History" by Iwan Bloch. These two sections gave the books a distinctive character, and along with the other contributions, all of them authoritative, made this system one of the great medical publications of all time. The work, moreover, may be read today with profit, and the "Introduction" and "History" are permanent contributions to literature.

D'Arcy Power also revised *Plarr's Lives of the Fellows of the Royal College of Surgeons of England* (1930), which consisted of two volumes. This work entailed a tremendous amount of careful research and is a monumental achievement. In research fields, moreover, Power edited a number of texts, such as John Arderne's two books, *Treatises of Fistula in Ano* (1910) and *De Arte Physicali et de Chirurgia* (1922).

In 1930, he came to the United States as visiting lecturer to the Institute of the History of Medicine of the Johns Hopkins University. His lectures were published in 1931 as *The Foundations of Medical History*, a small, but finely evaluated

document, particularly relating to the early history of medicine in England, a field in which he was a well-known authority. In 1931, his *Selected Writings* were issued, covering the period from 1877 to 1930. Finally, in 1939, a small book, entitled *A Mirror for Surgeons: Selected readings in surgery*, was published both in Great Britain and in this country.

D'Arcy Power was a man of great charm. He made friends readily. For years he was known to the students at St. Bartholomew's Hospital as "Sunny Jim." Although he was always cheery and never complaining, life dealt him many tragic blows. His only daughter died of whooping cough at the age of two, and his younger son was killed in World War I. During his last years he was saddened by the death of his wife. He kept up his activities, however, almost to the very end, occupying his house on Chandos Street, long a mecca for friends of medical history, throughout the bombing of London and up until the beginning of the present year. He then found it no longer safe to live there, or to keep his books, of which he had a great many, in such an exposed position. One of his last letters, stating that his books would be sold at Sotheby's auction room in London, was published in the May 17, 1941, issue of the *Journal of the American Medical Association*. A catalog of these books, recently received, shows that he had collected over the years a considerable number of important medical texts, some of which will find their way to this country.

Even in his later years, D'Arcy Power was an active person. He wrote, for example, many of the obituary notices of medical men in *The Times*, of London. This meant that he had to have the material readily at hand, for the notices were prepared in the course of a few hours. For the average man, this would have been impossible, but for the quick, surgically trained Power, nothing was too much of a task, and he turned out extraordinary obituary notes for the daily press, listing not only the important contributions that the deceased colleague had made to medicine, but also giving an estimate of the man's

character and the passing or enduring value of his work.

He kept up his cheerfulness to the end of his life. In a letter written last fall from London, before he had moved into the country, he noted in a postscript: "London has become very noisy. Fortunately, I have one deaf ear and I am not, therefore, much disturbed at night." For a man in his eighty-fifth year, living in the heart of London during the height of the blitzkrieg, to write in such a fashion characterizes this forthright gentleman. Surgeon, historian, biographer, lover of mankind, keen student of human nature, delightful correspondent and charming friend, D'Arcy Power leaves behind him many memories that will long be cherished by his friends, as well as a score of monumental contributions to medical literature. It was, indeed, characteristic of him that just before he died, he turned over to the Royal College of Surgeons a supplement to *Plarr's Lives*, bringing the necrologies up to 1940.

A fitting eulogy is contained in the final paragraph of his death notice in the May 31, 1941, issue of the *Lancet*.

And now that he has gone to his rest, he stands out not so much as a single individual, but as one of a chain of stouthearted English doctors continuing to serve mankind. For his father, coming from an old Yorkshire family, was Henry Power, the ophthalmic surgeon, a fine figure of a man. His son, D'Arcy II, is high up in the medical service of the Royal Air Force, and his grandson, D'Arcy III, is following the same profession. Here indeed is a family that have served their country well.

## MEDICAL EPONYM

### HUNTER'S GLOSSITIS

The strongly individualistic contributions of Dr. William Hunter (1861-), pathologist to the Charing-Cross Hospital, to knowledge of the nature and causes of pernicious anemia include numerous descriptions of the glossitis that is often identified by his name. The following quotation is from his article, "Further Observations on Pernicious Anaemia (Severe Cases): A chronic infective disease: Its relation to infection from the mouth and stomach: Suggested serum treatment," which appeared in the *Lancet* (1: 221-224, 296-299, 371-377, 1900):

... I was struck by the curious character of the sores on the tongue—localised inflamed patches sometimes showing vesicles filled with clear serum situated under the tip of the tongue, the inflamed areas shifting from time to time, with atrophic appearance of the intervening mucosa. The condition thus described is not one of ordinary stomatitis or glossitis such as one meets with as the result of the local irritation of decayed or irregular teeth. . . . Another feature I have had to note is what I may term the "periodicity" of the stomatitis—its variability from time to time, independently apparently of treatment, notably its greater severity at the outset of the disease, usually tending to subside or at least to give less discomfort as the disease advances.

R. W. B.

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

RAYMOND S. TITUS, M.D., *Secretary*  
330 Dartmouth Street  
Boston

#### CESAREAN SECTION, FOLLOWED BY FATAL SURGICAL SHOCK

A thirty-six-year-old primipara at term, because of fetal distress, was delivered by cesarean section when the cervix was almost fully dilated.

The prenatal care had been excellent. The patient had been under observation since the beginning of the third month, during which time the blood pressure was normal and the urine showed no albumin. At about four and a half months a large intramural fibroid was removed. This did not interrupt the pregnancy. The convalescence from this operation was stormy, and during the rest of the pregnancy the patient suffered from a secondary anemia, which was treated with ferrous sulfate and liver. The patient was in the hospital for observation several times during the last two months of her pregnancy.

Three weeks after the expected date of confinement, labor started, being induced by castor oil. Because she was rated as a bad surgical risk and because it was known that the baby was small, a test of labor was considered a conservative method of handling this particular patient. Two donors were in constant attendance during the labor, as was the physician. The labor was normal. At the end of nine hours, the cervix was practically fully dilated, with unruptured membranes. At this time, the membranes were ruptured and the head settled into the pelvis. Unfortunately, however, the

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

fetal heart became irregular and the rate slowed to about 90 beats per minute. Cesarean section was decided on, because of the irregular fetal heart and the patient's age. At operation, the cord was found to be tight about one shoulder, a condition that was probably the cause of the fetal distress. The amount of blood lost at operation was said to have been little. During operation, however, the patient's blood pressure could not be obtained and the pulse was very rapid. Intravenous glucose and 500 cc of blood were given at the end of the operation. The patient responded well but an hour later went into collapse and died.

*Comment.* Intramural fibroids that are removed during pregnancy may so injure the uterine wall that rupture during labor must be considered a possibility. Because of this, the patient was under close observation during labor, so that cesarean section could have been performed immediately, if there were any evidence of rupture.

When a patient is practically fully dilated and the fetal heart shows distress, it is always questionable whether cesarean section is a justifiable procedure. One would hesitate, knowing that the wall of the uterus had been weakened by a myomectomy, to perform a version. With full dilatation and the head in mid position, forceps in the hands of a skilled operator would probably have guaranteed a live baby about as well as laparotomy.

Shock is a peculiar thing. This patient apparently did not die of hemorrhage, but the laparotomy was more than she could stand. Everything was done that could have been done,—the patient was transfused, after which she rallied,—but in spite of this, she sank into collapse and died.

## COMMITTEE ON PUBLIC RELATIONS

It seems likely that many members of the Society would be interested in the following resolutions, which were recently passed by the medical staff of the Cape Cod Hospital and approved by its executive committee:

ELMER S. BAGNALL, *Secretary*

\* \* \*

WHEREAS, If we are not at war, we are in a state of grave emergency, and

WHEREAS, Both federal and state governments wish the regular forces strengthened by volunteers, and

WHEREAS, The enrollment of volunteers is hampered, first, by fear of personal injury and, second, by lack of measures to see that volunteers will be cared for, if injured in training or action, be it therefore

RESOLVED, That the Cape Cod Hospital and Cape Cod Hospital staff mutually agree to assure free hospitalization and medical care for any such volunteers to the limit of their resources, volunteers to be certified to have been injured in line of duty, while in training or on public service, and to include the State Guard, and be it further

RESOLVED, That should future plans or laws provide payment for such care and should payment be made for such care, the Cape Cod Hospital staff agrees to add such sums to the endowment fund of the Cape Cod Hospital.

## DEATHS

ANDERSON—BERTHA O. ANDERSON, M.D., of Pittsfield, died June 25. She was in her fifty-ninth year.

Born at Lawrence, Kansas, she received her degree from the University of Kansas School of Medicine in 1911. From 1911 to 1929 Dr. Anderson practiced general medicine, surgery and obstetrics in Lincoln, Illinois. From 1931 to 1935 she practiced in Lakewood, Ohio, specializing in diseases of the gastrointestinal tract, gynecology and proctology. She had taken postgraduate work at the New York Polyclinic Hospital and Harvard Summer School, and had done observation work at the Mayo Clinic in Rochester, Minnesota. She moved to Pittsfield in 1935 because of ill health.

Dr. Anderson was a member of the Massachusetts Medical Society and the American Medical Association. She was also a member of the National Women's Medical Association, the Women's Medical Association and the Lake Wood (Ohio) Medical Club.

A brother, a nephew and a niece survive her.

BURNETT—FRANK H. BURNETT, M.D., of Brockton, died June 21. He was in his seventy-sixth year.

Born in Guilford, Vermont, he attended Dartmouth College and received his degree from Dartmouth Medical School in 1890. Dr. Burnett was on the staff of the Brockton Hospital and was a former president of the Plymouth County Medical Society. He was a member of the Massachusetts Medical Society and the American Medical Association.

His brother survives him.

MCCROSSAN—CHARLES L. MCCROSSAN, M.D., of Somerville, died June 26. He was in his fifty-sixth year.

Born in Somerville, he attended Harvard University and received his degree from Harvard Medical School in 1910. At the time of his death he was a member of the Somerville Board of Health and was on the staff of the Somerville Hospital. He was a member of the Massachusetts Medical Society, the American Medical Association and the New England Obstetrical and Gynecological Society.

His widow, his father, a daughter, a son and two brothers survive him.

MULHOLLAND—BERNARD J. MULHOLLAND, M.D., of Lawrence, died April 16. He was in his fifty-ninth year.

Born in Lawrence, he received his degree from Biltmore Medical College in 1906, and started private practice in Lawrence.

He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow and two daughters survive him.

VICKERY—EUGENE A. VICKERY, M.D., of Wellesley, died June 22. He was in his sixty-third year.

Dr. Vickery received his degree from Harvard Medical School in 1903. He was a fellow of the Massachusetts Medical Society and the American Medical Association. At the time of his death he was Commander, Medical Corps, United States Navy (retired). He was a member of the Southeastern Surgical Congress and a fellow of the American College of Surgeons.

His widow survives him.

WALSH—JAMES H. WALSH, M.D., of Fall River, died May 14. He was in his fifty-eighth year.

Born in Fall River, he received his degree from the College of Physicians and Surgeons of Baltimore, Maryland, in 1910. He was a former president of the Fall River Medical Society, and was a member of the Advisory Board of the Union Hospital. For thirty years he was bacteriologist for the City of Fall River and was associate medical examiner for several years. For many years he was pathologist at the Union, St. Anne's and General hospitals, of Fall River, and the Newport Hospital of Newport, Rhode Island. At the time of his death he was on the Selective Service Board.

Dr. Walsh was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow, a daughter and a son survive him.

## CORRESPONDENCE

### NEW REGULATIONS IN REGARD TO COMMUNICABLE DISEASES

*To the Editor:* In 1938 an amendment to Section 6 of Chapter III of the General Laws authorized the Department of Public Health to make rules and regulations in regard to the control of communicable diseases. Such regulations were formulated and approved on August 9 of that year and were printed in the September 15, 1938, issue of the *Journal*.

In October of the same year, "infectious encephalitis" was made reportable, replacing the old terminology of "encephalitis lethargica." A note in regard to this change appeared in the November 10 issue of the *Journal*.

On May 13, 1941, further additions were made to the list of reportable diseases, and certain amendments were made in the isolation and quarantine requirements to bring them in line with the latest revision of the recommendations of the Subcommittee on Communicable Disease Control of the American Public Health Association. These changes are given below.

Printed copies of the revised regulations will be available for distribution in the very near future. The revised list of reportable diseases is also being reprinted and will be sent to every physician in the State.

I should also like to call attention to the fact that the rules and regulations for the treatment of persons exposed to rabies were amended so that the first sentence of Rule 2 reads as follows: "Antirabic vaccine and antirabic treatment shall be furnished by the board of health for all persons bitten on the head, or in cases with severe multiple lacerations." The amendment consists of the addition of the last phrase of this sentence.

PAUL J. JAKMAUH, M.D.  
Commissioner of Public Health

State House  
Boston

## CHANGES IN ISOLATION AND QUARANTINE REQUIREMENTS

### List of Reportable Diseases

Lymphocytic choriomeningitis and Weil's disease were added to the reportable list, and all forms of meningitis were made reportable. "Paratyphoid fever A and B" was changed to "Paratyphoid fever and all other *Salmonella* infections."

### Periods of Isolation and Quarantine

*Chicken pox.* (Column 2.) Amended to read as follows: "One week from appearance of eruption and thereafter until crusts have disappeared, provided that total period of isolation shall not exceed fourteen days."

*Cholecystitis of typhoid origin.* (Columns 4 and 5.) Omitted "No restrictions" and substituted "Same as typhoid fever."

*Diphtheria.* (Column 4.) Omitted "or on the basis of a previous attack of the disease."

*Dysentery, amebic.* (Column 2.) Omitted "Same as typhoid fever" and substituted "No restrictions except for foodhandlers, who shall be kept from their occupations until three successive negative stool examinations, secured at intervals of not less than three days apart, shall have been obtained." (Column 3.) Omitted "Note 3" and substituted "No restrictions except for foodhandlers, for whom restrictions are same as for case."

*Dysentery, bacillary.* (Columns 4 and 5.) Omitted "No restrictions" and substituted "Same as typhoid fever."

*Infectious encephalitis.* (Column 1.) Order of words changed to "Encephalitis, infectious," and placed in table immediately after "Dysentery, bacillary."

*Lobar pneumonia.* (Column 1.) Order of words changed to "Pneumonia, lobar," and placed in table immediately after "Plague."

*Lymphocytic choriomeningitis.* (Column 1.) Placed in table immediately after "Leprosy." (Column 2.) "Until recovery." (Columns 3, 4 and 5.) "No restrictions." (Column 6.) "No."

*Measles.* (Column 5.) Changed "Note 7" to read "Note 8."

*Meningococcus meningitis.* (Column 1.) Order of words changed to "Meningitis, meningococcal."

*Ophthalmia neonatorum.* (Column 2.) Amended to read: "One week after subsidence of symptoms. In gonococcal ophthalmia, thereafter until two successive smears from each eye at an interval of not less than forty-eight hours are negative for gonococci."

*Paratyphoid fever.* (Column 1.) Omitted "A and B" and substituted "and all other *Salmonella* infections." (Columns 4 and 5.) Omitted "No restrictions" and substituted "Same as typhoid fever."

*Pfeiffer bacillus meningitis.* (Column 1.) Amended to read: "Meningitis, other forms, such as Pfeiffer bacillus, pneumococcal, streptococcal, etc." and placed in table immediately after "Meningitis, meningococcal." (Column 2.) Omitted "No restrictions" and substituted "Until recovery."

*Tuberculosis.* (Column 3.) Omitted "No restrictions" substituted "Note 7."

*Typhoid fever.* (Columns 4 and 5.) Omitted "No restrictions" and substituted "No restrictions provided contacts can be relied upon to observe precautions outlined by board of health and provided at least one satisfactory stool specimen is submitted for examination."

*Weil's disease, infectious jaundice due to *Leptospira icterohemorrhagiae*.* (Column 1.) Placed in table imme-

diately after "Undulant fever" (Column 2) "Until recovery" (Columns 3, 4 and 5) "No restrictions" (Column 6) No"

#### Notes

**Note 3** In line 1 substituted household for "family" Omitted the words "amebic or" and substituted the word "fever" for the phrase "A or B" Added the following sentence to the note "Foodhandlers living in a household with a recovered case which continues to excrete typhoid bacilli after convalescence shall be excluded from their occupations unless they have been inoculated with typhoid vaccine within two years"

**Note 6** Amended to read "Patients with open tuberculosis should in most cases receive sanatorium treatment both for the benefit of the individual and the protection of his family Those who remain in their homes shall observe all precautions necessary to prevent infection of the members of their families and of others with whom they may come in contact This shall include approved methods of collection and disposal of the sputum the sterilization of any articles of clothing and of toilet articles which may become contaminated by the sputum the use of separate dishes and eating utensils and proper sterilization of the same The patient should sleep in a separate room For details concerning precautions in home care a pamphlet of the Massachusetts Department of Public Health entitled *Home Care of Tuberculosis Patients* is available

"As soon as a diagnosis of tuberculosis has been established arrangements should be made for the examination, including an x ray of the chest, of all members of the immediate family and of other persons with whom the patient has been in close contact If the family cannot afford x ray examination by a private physician, facilities are available through the various state, county and municipal sanatoria Persons with suspicious findings and those who have had contact with a tuberculous patient should be kept under medical observation as long as advised by the physician It is the responsibility of the local board of health to provide hospital care for cases of tuberculosis, when needed, and to see that contacts are examined where such examinations have not been made through a private physician

"When a case is reported the public health nurse representing the board of health should visit the patient's home She should instruct the family in the sanitary precautions described above, see that arrangements are made for the examination of contacts and if necessary provide transportation to the place where they are to be x rayed and should aid the patient in obtaining admission to a sanatorium if this has been recommended by his physician

"Hereafter, the nurse should make visits to the home at least once in six months to determine whether the patient has moved, whether the above mentioned precautions are still being observed and whether any new measures are needed to control the spread of the disease If the patient has moved in another town or state, the Massachusetts Department of Public Health should be notified In cases where the physician wishes to exercise complete supervision, the nurse should obtain such information from him

"The only acceptable reasons for the board of health failing to exercise the supervision outlined above are refusal of the family physician to permit periodic visits by the nurse or placing of the patient's name on an 'inactive list' as a result of examination, including x ray

"No person who has or who has had tubercle bacilli in the sputum or other bodily discharges shall be allowed

to engage in teaching, nursing, dairying or occupations involving food handling or the care of children until he has received a certificate from the board of health stating that his employment would not be dangerous to the public health"

**Note 7** Substituted "Persons living in a family in which a case of tuberculosis exists or has existed within two years, and whose occupations involve food handling or contact with children, shall be required to have an x ray of the chest to determine whether they shall be allowed to continue in such occupations"

**Note 8** Former Note 7, renumbered

#### ARTICLES ACCEPTED BY THE COUNCIL ON PHARMACY AND CHEMISTRY AMERICAN MEDICAL ASSOCIATION

*To the Editor* The following products have been accepted by the Council on Pharmacy and Chemistry since May 1, 1941

##### Armour Laboratories

Suprarenalin Solution 1 1000, 5 cc vial (for hypodermic use)

##### Geo A Breen & Co, Inc.

Tablets, Ascorbic Acid—Breen, 25 mg

Tablets, Ascorbic Acid—Breen, 100 mg

##### Cutter Laboratories, Inc.

Sobisminal Solution—Cutter, 50 cc bottle

##### Drug Products Co, Inc.

Pulvoids Thiamine Hydrochloride, 1 mg

Hyposols Solution of Thiamine Hydrochloride Crystals, 666 mg per cc, 1 cc ampuls and 10 cc and 30 cc vials

Hyposols Solution of Thiamine Hydrochloride Crystals, 10 mg per cc, 1 cc ampuls and 10 cc and 30 cc vials

Hyposols, Solution of Thiamine Hydrochloride Crystals, 3333 mg per cc, 1 cc ampuls and 10 cc and 30 cc vials

Hyposols, Solution of Thiamine Hydrochloride Crystals, 50 mg per cc, 10 cc ampuls and 10 cc and 30 cc vials

Hyposols, Solution Procaine Hydrochloride 2 percent, 2 cc ampuls

##### Endo Products, Inc.

Ampoules, Epinephrine in Oil 1 500—Endo, 1 cc

Tablets, Nicotinic Acid—Endo, 50 mg, scored

Tablets, Nicotinic Acid—Endo, 100 mg, scored

##### Flint, Eaton & Co

Tablets, Sulfanilamide, 1 gr

Tablets, Sulfanilamide, 77 gr

Tablets, Sulfapyridine, 05 gm (77 gr)

Sulfathiazole Tablets, 05 gm (77 gr)

##### Lederle Laboratories

Tablets, Aminophyllin—Lederle, 02 gm (3 gr)

##### Elk Lilly & Company

Tablets, Sulfathiazole—Lilly, 025 gm (3/4 gr)

Tablets, Sulfathiazole—Lilly, 05 gm (7 1/2 gr)

##### National Drug Company

Tablets, Sulfanilamide, 1 gr

Tablets Sulfanilamide, 7 1/2 gr



Schieffelin & Co.

Sulfanilamide Tablets,  $7\frac{1}{2}$  gr.

Smith-Dorsey Company

Tablets, Sulfapyridine, 0.5 gm. (7.7 gr.)

Frederick Stearns & Co.

Ascorbic Acid Tablets—Stearns, 50 mg.

Ascorbic Acid Tablets—Stearns, 100 mg.

Upjohn Company

Typhoid Vaccine—Upjohn, six  $2\frac{1}{2}$ -cc. vials, package

Tablets, Sulfapyridine—Upjohn, 0.5 gm. (7.7 gr.)

Tablets, Sulfathiazole—Upjohn, 0.5 gm. (7.7 gr.)

Winthrop Chemical Co., Inc.

Pontocaine Base Eye Ointment

OFFICE OF THE COUNCIL

By: C. C. Bean

535 North Dearborn Street  
Chicago, Illinois

## REPORTS OF MEETINGS

### HARVARD MEDICAL SOCIETY

A regular meeting of the Harvard Medical Society, held at the Peter Bent Brigham Hospital on April 8, was inaugurated by the usual presentation of a case.

A middle-aged woman had experienced a fall eight months before admission, with the subsequent development of headache and dizziness. She had had known hypertension for two years. For two weeks prior to entry, there had been extreme vertigo, with a marked tendency to stumble to the left and with weakness of the right side. Physical examination was remarkable chiefly for moderate cardiac enlargement and hypertension (160 systolic, 100 diastolic). On neurologic appraisal, there was weakness of the right arm and leg associated with diminished tendon reflexes. Poor co-ordination of the left arm and leg was noted. Pain sense was diminished on the left trunk and leg. All laboratory data, including examination of the cerebrospinal fluid, were negative. The electroencephalogram revealed diffuse abnormalities from all areas, and a cystometrogram indicated the presence of a cord bladder.

Dr. Soma Weiss stated that this was an example of an unusual syndrome, thrombosis of the inferior cerebellar artery—in this case, on the left side. This condition results in pyramidal-tract signs on the opposite side, and cerebellar and sympathetic manifestations on the homolateral side. Dr. E. A. Stead, Jr., remarked that the disease is rare in that the symptoms and signs result from central rather than peripheral paralysis. Therefore, a dissociation of symptoms, with some normal as well as abnormal responses, may result.

The speaker of the evening was Dr. Walter F. Dearborn, of Harvard University, whose subject was "Disabilities in Reading and Their Remedying." In introduction, it was emphasized that these difficulties may occur at any level of educational life and may cause late as well as early failures. A welter of causes has been suggested, which may be environmental, educational or organic. Poor training, large classes, absence from school, faulty home facilities and so forth may contribute a share of reading disability. Organic causes, such as difficulty with articulation, deviations in eye and hand dominance and anisopia, probably function largely as ini-

tial handicaps that trip only a few students, whereas multiple structural changes are frequent. Visual acuity and eye-muscle imbalance are becoming less popular as causative factors.

Dr. Dearborn believes that laterality and mixed dominance play a role. Even opponents agree that left-eye dominance favors right-to-left eye movements. Although something may be gained by waiting in such cases, Dr. Dearborn suggests "changing the menu" in the meantime to avoid the early emotional upsets that may occur during the process of expectant waiting. Furthermore, time alone will not always bring the desired results.

A study of left ocular and manual dominance indicates that persons with such findings are retarded in about 40 per cent of cases, but that the greatest degree is noted in those with mixed dominance of hand and eye. This may cause an aversion to reading if nothing is done at an early date. This aversion may be accentuated in an intelligent person who has some other special skill, and in such cases it is particularly worth while to treat left lateral or mixed dominance.

Anisometropia, with poor fusion of the images of the two eyes, causes an extra effort and makes reading a difficult task. This was present in 50 per cent of extreme cases of disability, as against 23 per cent in a control group. It is probably a factor in certain cases, therefore, but admittedly not an insurmountable one. In many cases of reading disability, one may discover a chief cause, but just about as frequently multiple well-recognized causative factors are present.

The chief remedy is to have only one capable instructor with a unity of purpose. Too many schools merely complicate matters, and no one is able properly to treat cases of reading disability, even when the diagnosis is made. The problem is most acute in the young, but is far from absent at college age. Freshman training at Harvard University is now accomplished by means of motion pictures graded for speed. It has been found possible in this way to increase the speed and accuracy of reading and to elevate the college grades as compared with controls. More recently, stress has been laid on comprehension rather than mere reading ability.

The discussion was opened by Dr. Edwin M. Cole, of Harvard Medical School. For organic disease or injury to cause aphasia the lesion must be unilateral on the dominant side. He has been impressed with the hereditary aspects of the dominance problem and the high incidence of stuttering, left-handedness and reading disability in such families.

Dr. Virgil G. Casten stated that an ophthalmologist's sole purpose in cases of reading disability should be to rule out organic eye disease, although even such seemingly serious findings as anisocoria seldom cause such difficulty of themselves.

In conclusion, Dr. Dearborn stated that anyone with reading disability can be either taught or improved if enough time and patience are employed.

### EVANS MEMORIAL LECTURE

At a Robert D. Evans Memorial Lecture at the Evans Memorial, Massachusetts Memorial Hospitals, on March 28, Dr. Allen O. Whipple, of Columbia University, discussed "Certain Splenopathies in Relation to the Vascular Bed of the Spleen." The discussion was based on 483 splenopathies observed in the Combined Spleen Clinic, of which 237 were operated on, with a mortality rate of 8 per cent.

There has been much discussion about the character of the vascular bed of the spleen, some observers considering

it an open system wherein there is no actual connection but merely a vascular bed between the arterioles and venules. The opposite view of a closed system with terminal arterioles communicating directly with the venous sinuses has been proposed, and some observers believe in a combination of the two extreme views. Between 1936 and 1938, it was considered that ample evidence was at hand to indicate that a closed system obtained under normal conditions, and that any suggestion of a vascular bed was the result of handling or improper technique. An improvement of the technical details whereby the spleen may be directly observed in its functioning physiologic state seems to contradict these previous findings, and it is now believed that this new method of refractility may make anatomic structure and physiologic function coincide. At any rate, certain positive statements can be made: the pulp spaces are the chief, if not the only, link between the arterioles and veins; these are variable in size and shape, with interconnections, their size is such that cells as well as fluid can pass through; they may dilate to several times the size of an erythrocyte or contract to almost nothing, the spaces are the only site of circulation and storage of and contact with phagocytes, serving as a means of bringing the circulating blood in contact with the pulp-space cells for phagocytosis and destruction of erythrocytes. Only a few important conditions associated with this pulp system were discussed.

In chronic microcytic hemolytic anemia, there may be a hemolysis at work, or inferior erythrocytes in the form of spherocytes, which are easily destroyed may be present. This was not debated. The importance of the spleen in this condition is proved by the effect of splenectomy. Microscopically there is engorgement of the pulp spaces with spherocytes, and the venous sinuses are collapsed by the pressure of the distended spaces. Since the spherocytes are unable to pass owing to their inflexible nature and their lack of rouleaux formation they are exposed for longer periods to any hemolyzing factor in the pulp-space walls, and are either sensitized or directly destroyed by the hemolysis. There is evidence of an enhanced fragility and of a larger number of such cells in the arterioles and pulp spaces than in the venules. This indicates that it is in these spaces rather than in the venous sinuses that the cells are in proximity with phagocytes.

Hypertensive splenomegaly, which is considered a congestive disease, is usually signified clinically as Banti's syndrome of hepatosplenomegaly. The present concept of this condition, which also includes the finding of anemia, leukopenia and gastrointestinal hemorrhages, includes many cases not originally considered by Banti and excludes some cases following the original description. This syndrome may be caused by any obstruction to flow within the portal vein but only if there is a gradual increase of portal vein pressure while the peripheral venous pressure remains essentially unchanged. The site of obstruction may be intrahepatic or extrahepatic. Sixty-eight per cent of 140 cases were directly attributable to cirrhosis of the liver. The amount of hypertension and splenomegaly is proportional to the type of cirrhosis. That due to *Schistosomum mansoni* causing the greatest degree. This can be reproduced in dogs by the injection of silica particles in the portal vein over a period of about sixteen months. Laennec's cirrhosis or periportal fibrosis causes a variable degree of hypertension and these patients are prone to succumb to liver insufficiency, the chief pathological findings being in the lobules rather than in the periportal areas. Among the extrahepatic causes of

the Banti syndrome may be mentioned a traumatic pancreatic cyst wherein operation effected a cure. In infants and children a congenital block of thrombosis may imitate the condition. Early operation should be carried out and a liver biopsy always performed, for only those without cirrhosis of the liver may be cured. No subsequent cirrhosis has been known to develop if there was none at operation, whereas patients with cirrhosis have recurrences of all manifestations. Histologically, these spleens have distended venous sinuses, diminished pulp spaces and fibrosis.

## BOOK REVIEWS

*The Head and Neck in Roentgen Diagnosis* By Henry K. Pincus MD, Eugene P. Pendergrass, MD, and J. Parsons Schaeffer, MD, PhD. 4<sup>th</sup> ed., cloth, with 1251 illustrations. Springfield Illinois: Charles C. Thomas, 1940. \$12.50.

This book is undoubtedly the best textbook of its kind in the English language. It is encyclopedic in character and is profusely illustrated with reproductions of roentgenograms, anatomic illustrations, drawings, photographs and even a few colored plates. The compilation and arrangement of such a monumental work must necessarily mean many months but years of arduous labor, and the painstaking accuracy with which the vast volume of material is presented is a tribute to the diligence and indefatigable attention of the authors. The book is a real monument to the memory of Henry K. Pincus, the senior author, who died while it was still in embryo, one stage and the major credit should go to the junior author, E. P. Pendergrass, who carried it to completion, with the help of the associate author J. Parsons Schaeffer, who has added the valuable anatomic groundwork on which the roentgenographic material is based. The book covers every conceivable method, procedure and process in roentgenography as well as the rules and precepts of diagnosis. It is important to know the methods of examination and the technical aids that can be used as well as the normal anatomic relations of each part examined. Both features are well covered.

The subject matter is unusually wide in scope, since the authors cover not only the skull and brain which alone would make quite a monograph but also the sinuses, the teeth and jaws, the mastoids, the eyes, nose and laryngeal passages and the neck—not only the cervical spine but also the soft tissues of the neck and the cervical spinal cord. It is indeed a very comprehensive and complete book and very accurate and reliable, and yet there are a few faults to be found since no book is ever quite perfect. One might grade it ninety-nine per cent and thus take away emphasis from the one per cent of criticism. The reviewer has observed only two major faults. The anatomy, although detailed and no doubt quite accurate, might well have been correlated better with the roentgenologic viewpoint and the descriptive text. As written the anatomic descriptions stand out like islands in the roentgenologic current. The other minor defect is the fact that quite a few of the illustrations were apparently made from old films or plates and are lacking in sharpness of contrast and detail such as everyone expects routinely today. This is perhaps unavoidable, since one cannot expect to accumulate perfect examples of the thousand and one varieties of disease in a year or two. The authors have wisely borrowed illustrations from their confreres and have been most careful to give due credit for each one used.

One should make particular note of the fact that all roentgenograms are printed as negatives, that is, in their original whites and blacks—a laudable procedure, and one that other roentgenologic textbooks would do well to emulate. Another very commendable feature is the extensive and complete index, covering seventy-two pages. The index of such a book must necessarily be one of its most important parts, and yet a proper index is all too frequently slighted. Not so in this book, although there are a few errors and omissions—for example, “glioma” refers only to the description of calcification in the gliomas and not to the classification of gliomas heading that section. One might add other minor criticisms, such as the charge that the authors’ classification of brain tumors as “parasellar,” “metasellar” and so forth is unclear and not useful, or that pathology and clinical correlation have been slighted for anatomy, but to do so would be to emphasize the one per cent of criticism and slight the ninety-nine per cent of commendation and approbation.

The mechanics of the book are excellent—the typography is clear, the illustrations are as good as any in American textbooks (and better than most), the paper is of very good quality, and the whole make-up is highly commendable. The publishers as well as the authors are to be congratulated. On the whole, this book is valuable, comprehensive and accurate, and should be in every roentgenologist’s office—on his desk for everyday use.

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*De morbis artificum* [Disease of Workers]. A diatribe by Bernardini Ramazzini. The Latin text of 1713—revised, with translation and notes. By Wilmer Cave Wright. 8°, cloth, 549 pp., with 3 illustrations. Chicago: University of Chicago Press, 1940. \$5.00.

One of the classic texts of medicine is the book by Ramazzini, first published in 1700, on occupational diseases. An English translation has long been needed, for the book has not been put into that language since the eighteenth century, and at that time only part of it was translated. In many cases, moreover, the early translators paraphrased the text and omitted what they thought superfluous or obscure. Now, Dr. Wright, emeritus professor of Greek at Bryn Mawr College, and well known for her fine translation of Fracastorius’ *De Contagione* (1546), has made an excellent English translation from the Latin text of 1713. She has, moreover, added numerous notes, and provided a sixty-four-page introduction, giving not only the history of the man but details in regard to the various printings of the book itself. Such a book must naturally be in the historical collection of every medical library. The volume is one of a series issued on the history of medicine under the auspices of the Library of the New York Academy of Medicine. Not the least useful of the series of texts published under their auspices is this book by Ramazzini.

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*Doctor in Arabia*. By Paul W. Harrison, M.D. 8°, cloth, 303 pp., with 9 illustrations. New York: The John Day Company, 1940. \$3.00.

Harrison, a graduate of Johns Hopkins, went to Arabia as a missionary doctor after finishing his internship in Boston, and settled in Muscat, on the Persian Gulf, one of the driest, hottest and most inaccessible corners of the world. Muscat was the center of the contraband traffic in ammunitions, and Harrison found a million rifles for sale in the warehouses of that little city. It was also the port

for the export of Oman dates. When Harrison set up his hospital, it is interesting to note that operation for strangulated hernia was one of the commonest.

Harrison describes his patients, the public-health problems and economic and social conditions in Oman, and the daily life of a splendid, high-minded missionary doctor, working against heavy, environmental odds. He looks forward to a time when the government of Oman will organize a health service for the whole country. This would be the only way to fight the diseases commonly met with in Dr. Harrison’s hospital: malaria, Madura foot, trachoma, syphilis, gonorrhea and leprosy. The members of the medical staff should be natives, and the hospital should be a department of the government, with community support behind it. One is convinced that Dr. Harrison had made out a case and that his book points the way to the value of social medicine in the isolated corners of the world.

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*Manual of Physical Diagnosis, with Special Consideration of the Heart and Lungs*. By Maurice Lewison, M.D., and Ellis B. Freilich, M.D. In collaboration with George C. Coe, M.D. 8°, cloth, 317 pp., with 75 illustrations. Chicago: The Year Book Publishers, Incorporated, 1941. \$3.00.

The appearance of so many new textbooks of physical diagnosis during the last few years may be attributed to the natural desire of each publishing company to find and sell a text that will be accepted as standard all over the country. These books generally show little originality, and vary from one another only in the degree of elaboration and pictorial illustration with which they present the old facts of physical examination combined with a certain amount of electrocardiography, and the discussion of a few groups of clinical syndromes, particularly “diseases of the chest and circulatory organs.” Some of them, such as those offered by Martini, by Buck and by Clendening, limit their subject matter to the noninstrumental examination of the patient. This book is an example of the simpler type of text, and is to be recommended on this account.

There is remarkably little fault to be found in respect to its accuracy, although the old American legend of physiologic dullness of the apex of the right lung is dutifully repeated. A defect is that bibliographic references which might aid the student to develop the habit of consulting original sources are entirely lacking.

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*Bacteriology in Neuropsychiatry: A survey of investigations concerned with the specific role of infectious and immune processes*. By Nicholas Kopeloff, Ph.D. 8°, cloth, 316 pp., with 11 tables. Springfield, Illinois: Charles C Thomas, 1941. \$4.50.

The reviewer has rarely met with a book that seems to have as slight a value to the medical profession as this one. All the material of any worth is easily found in common medical literature. The second half of the volume is padded with speculations of no apparent scientific value, and there are large sections on treatment, which seem to be wholly out of place in a book on bacteriology. The literature is widely quoted, but with little discrimination. The book, unfortunately, is finely published, and the splendid reputation of the publisher may catch the unwary.

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## POLYNEURITIS WITH FACIAL DIPLEGIA\*

### A Clinical Study

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**P**OLYNEURITIS with facial diplegia, or so-called "infectious neuritis" or "neuronitis," has attracted considerable attention since 1908, when Laurens<sup>1</sup> published his Paris thesis, entitled "*Des diplegies faciales au cours des polynévrites*."

The cause of this type of polyneuritis is obscure. Since the onset of the neuritic symptoms in many of the cases followed an upper respiratory infection, it was thought that a filterable virus might be the causative agent, but all recent attempts to isolate a virus from these cases have been unsuccessful. The pathology has not been adequately studied because until recent years the disease has been relatively benign. From the reports of the few cases that have been studied, the pathology consists chiefly of a degeneration of the myelin sheaths of the peripheral nerves, with slight changes in the axis cylinders.<sup>2-3</sup> Inflammatory reaction in the nerves may or may not be present. The central nervous system is not affected to any appreciable extent, except for swelling and chromatolysis (axonal reaction) of the motor cells in the medulla and in the ventral horns of the spinal cord.

Indeed, there is some doubt whether these cases constitute a true disease entity, since facial diplegia may be present in polyneuritides of diverse causes and absent in otherwise typical cases of infectious polyneuritis. The clinical picture is sufficiently characteristic in the majority of the reported cases<sup>2-3</sup> to justify the conviction that there must be a common etiologic factor.

Since there are few reports in the literature of large series of cases followed for any length of time, it was thought advisable to present an analy-

sis of the 26 cases that have been studied on the neurologic wards of the Boston City Hospital in the last ten years. Particular attention is given to the status of the patients who recovered, and an attempt is made to evaluate the factors in the history and the clinical findings that are significant in regard to recovery or death. A complete description of the pathological findings in the fatal cases that came to necropsy will be presented in a subsequent publication from this clinic.

A summary of the history, examination and final status of the 26 cases is given in Table 1. The complete record of two typical cases is also presented.

### ANALYSIS OF CASES

*Age and sex.* The disease is commonest in young adults or in early middle age. The extreme age limits in our series were two and seventy-eight, with an average of thirty-five years. The division of the 26 cases according to age decades was as follows: first, 2; second, 2; third, 6; fourth, 8; fifth, 5; sixth, 1; and eighth, 2.

Nineteen of the 26 patients (73 per cent) were males, and 7 were females.

*History of infection prior to onset of neuritis.* In 13 (50 per cent) of the patients, there was a history of preceding infections. An upper respiratory infection, usually of relatively mild character, had preceded the neuritis in 10 patients. In the 3 remaining patients, 1 had an acute gastroenteritis, 1 a pyelitis, and 1 a poorly defined illness characterized by epistaxis, malaise and fever. The period between the preceding infection and the onset of the neuritic symptoms varied between two and twenty-eight days. This interval was less than two weeks in 10 of the 13 cases.

*Mode of onset.* In 15 of the 26 cases the symptoms were generalized at the onset. This is somewhat contrary to the usual conception. However,

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TABLE 1. *Summary of Records of 26 Cases of Polyneuropitis with Facial Diplegia.*

CASE No.	AGE	SEX	ADMISSION DATE	DISCHARGE DATE	PRECEDING INFECTION	LOCATION OF INITIAL SYMPTOMS	RESPIRATORY PARALYSIS	CRANIAL-NERVE PARALYSIS	SENSORY CHANGES	DEEP REFLEXES	PRESSURE mm. of H <sub>2</sub> O	CEREBROSPINAL FLUID CELLS per cu. mm.	PROTEIN mg./100 cc.	COLLOIDAL GOLD	OUTCOME
1	3	M	4/10/36	5/7/36	+	Arms and legs	+	7	0	Absent	100	1	68	012321100	Died
2	35	F	11/10/35	11/11/35	0	Legs	+	0	0	Decreased	110	6	44	5555432100	Died
3	36	F	6/10/40	7/11/40	0	Arms and legs	0	7	+	Absent*	155	30	136	0000000000	Improved†
4	70	M	1/11/31	2/10/34	+	Legs	0	3.5-7.9-10	0	Absent*	112	13	54	0112110000	Improved†
5	22	M	6/23/38	6/30/38	0	Arms and legs	+	7.9-10	0	Absent	60	150	200	1111233210	Died
6	15	F	4/7/38	4/19/38	0	Legs	+	7.9-10	+	Absent	175	11	9	0000000000	Died
7	25	M	1/24/38	2/3/38	+	Arms and legs	+	7.9-10-11	+	Absent	90	2	146	0000111000	Died
8	78	M	9/20/37	9/24/37	0	Legs	-	7.9-10	+	Absent	150	0	174	0012100000	Died
9	2	M	7/21/34	8/13/34	+	Legs	0	7	0	Absent*	—	6	363	1111233321	Recovered (6 weeks)
10	43	M	3/8/35	5/4/35	+	Arms and legs	0	0	0	Absent	220	5	170	011233221	Slight residuals
11	23	M	8/14/35	11/22/35	+	Legs	0	5.7-9-10	+	Absent	110	44	168	0123332210	Recovered (3 years)
12	34	F	3/6/40	3/21/40	+	Arms and legs	+	7.9-10	0	Absent	180	0	190	0000000000	Died
13	49	M	2/25/40	2/29/40	+	Legs	+	7.9-10	0	Absent	140	0	28	0000000000	Died
14	28	F	10/20/39	10/24/39	0	Arms and legs	+	7.9-10	+	Absent	150	2	138	0001221100	Died
15	22	M	10/12/35	11/22/35	0	Legs	0	7	0	Decreased	150	11	156	0122211000	Died
16	37	M	8/10/34	9/18/34	+	Arms	0	5.7-11-12	0	Absent	110	2	25	0010000000	Improved†
17	33	M	1/25/35	5/19/35	+	Arms	+	7.9-10	0	Absent	140	3	37	0000111000	Slight residuals
18	48	F	1/20/34	2/8/34	0	Face	0	5.7-9-10-11-12	0	Decreased	110	4	39	0001221100	Improved†
19	18	M	11/5/30	2/28/31	0	Arms and legs	0	7	+	Absent	300	—	780	—	Recovered (6 months)
20	35	M	4/23/34	6/10/34	+	Legs	0	7	+	Decreased	150	10	98	0011221100	Improved†
21	33	M	9/2/36	11/23/36	0	Legs	0	0	0	Absent	85	0	93	0011110000	Marked residuals
22	52	M	12/12/36	1/20/37	+	Legs	+	7.9-10-11	0	Absent	65	—	84	—	Improved†
23	32	F	1/25/34	2/8/34	+	Arms and legs	+	6.7-9-10-11-12	+	Absent	190	3	354	122234322	Died
24	49	M	10/17/34	12/5/34	0	Legs	0	0	+	Absent	130	0	98	0012232100	Improved†
25	45	M	4/16/40	4/17/40	0	Legs	+	7.9-10-11	0	Absent	120	0	37	0000000000	Died
26	28	M	6/21/30	8/9/30	0	Legs	0	5.7-9-10	0	Absent	240	0	399	000001233	Recovered (3 years) ...

\*Decreased in arms, absent in legs.

†Improved on discharge; no follow-up made.

when the illness began with localized involvement it was predominantly in the lower extremity (10 cases).

**Temperature and pulse.** In only 5 patients was the admission temperature 100°F. or above, and in these the temperatures were 100.4, 100, 100, 104 and 102°F. The temperature usually became normal in a few days.

Pulse rates were but moderately elevated, averaging approximately 95 on admission. However, in the fatal terminations there was a rise in pulse rate. When the use of a respirator became necessary it was not unusual for the pulse to become rapid, weak and thready, frequently faster than 150 a minute.

**Cranial-nerve involvement.** The cranial nerves were involved in 22 patients (85 per cent). The facial nerve was involved on both sides in all these patients. The frequency of this involvement alone and in combination with other cranial nerves is shown in Table 2. The infrequency of

patient. The response to plantar stimulation was usually absent, or there was a slight downward flexion.

**Respiratory failure.** In 13 patients, sufficient embarrassment of respiration occurred to necessitate the use of a respirator. The interim between onset of illness and the use of the respirator varied from two to twenty-one days, with an average of twelve days.

#### LABORATORY DATA

**White-cell counts.** The white-cell counts varied from 6200 to 22,000. Counts above 10,000 were recorded in 9 out of 22 cases.

**Red-cell counts.** Red-cell counts varied from 2,900,000 to 6,000,000. Four patients had counts below 4,000,000.

**Hemoglobin.** The hemoglobin varied from 58 to 108 per cent, with an average of 89 per cent. Only 2 patients had a hemoglobin below 70 per cent.

**Urine.** Routine tests on the urine were negative in all but 5 patients; in 4 of these the urine contained a slight amount of albumin, and in 1 a large amount of albumin and a few white cells.

**Cerebrospinal fluid.** The cerebrospinal fluid was examined one or more times in all 26 patients. The figures given below are an analysis of the findings at first examination.

The pressure varied between 70 and 300 mm. of water, with an average of 140 mm. A pressure greater than 200 mm. was recorded in only 3 patients.

The cell count of the fluid was normal (less than 5 per cubic millimeter) in 14 patients. There were between 5 and 20 cells in the fluids from 6 patients. Cell counts greater than 20 were recorded in only 2 patients (40 and 150, respectively).

TABLE 3. The Protein Content of the Cerebrospinal Fluid Removed at First Puncture.

PROTEIN CONTENT mg/100 cc.	No. of Cases
6-30	3
30-45	4
45-75	3
75-200	12
200 or above	4*

\*354, 363, 399 and 720 mg

The cells present were of the lymphatic series. When cells were found in the fluids obtained at first puncture, there was a tendency for them to decrease in number with subsequent punctures.

The protein in the fluids varied from 9 to 750 mg. per 100 cc., with an average of 157 mg. The range of values found is shown in Table 3. The

TABLE 2. Involvement of the Cranial Nerves.

NERVES INVOLVED	No. of Cases
Seventh alone	6
Seventh with tenth	5
Seventh with ninth and tenth	2
Seventh with fifth, ninth and tenth	2
Seventh with fifth, ninth, tenth, eleventh and twelfth	2
Seventh with ninth, tenth and eleventh	2
Seventh with third, fifth, ninth and tenth	1
Seventh with fifth, eleventh and twelfth	1
Seventh with sixth, ninth, tenth, eleventh and twelfth	1

involvement of oculomotor nerves is conspicuous, being present only twice. In none of our cases was papilledema noted.

**Muscular system.** Motor weakness was marked, especially in the proximal joints of the limbs, and in most cases the upper and lower extremities were involved to an equal degree. The trunk muscles were also weak in the majority of the patients.

**Sensory changes.** Disturbance of superficial cutaneous sensation (touch, pinprick, temperature) was present in only 7 patients. This was usually of a mild degree, consisting of hypesthesia of a glove-and-stocking type in 4 patients, a hypesthesia in the lower extremities and trunk in 1 and a severer loss (anesthesia) in the entire lower extremities in 1. There was a slight or moderate diminution of vibratory sense in 5 patients, and position sense in the legs was lost in 1. Muscle tenderness was found in 8 of the 26 cases, and nerve-trunk tenderness in but 1.

**Deep reflexes.** The tendon reflexes were absent in all four extremities in 19 patients, diminished in 4 and diminished in the arms and absent in the legs in 3. Abdominal reflexes were usually absent. The Babinski reflex was not found in any

protein was within normal limits (less than 45 mg. per 100 cc.) in 7 cases, moderately increased (45 to 75 mg.) in 3 and greatly increased in the remaining 16.

Since there has been an attempt to explain the occasional presence of normal protein content on the basis of a time factor,—that is, when the puncture was performed too soon after the onset of the disease for the protein to be elevated,—the period between the onset of symptoms and the punctures was determined. For those patients with a protein below 90 mg. per 100 cc., the range was found to be from three to thirty-five days, with an average of fourteen days. Of the group with an elevated protein, the range was from two to two hundred and seventy days, with an average of twenty-eight. If the case with an interval of two hundred and seventy days is eliminated, the average for this group becomes fifteen days. There is not enough evidence to rule out this factor, but the figures suggest that the time element is of no importance.

The sugar content of the fluids was slightly decreased in 1 patient of the 14 in whom determinations were made; 9 were within normal limits, and 4 slightly increased. The lowest sugar was 39 mg. per 100 cc., the highest 168 mg. The average for the 16 was 70 mg.

The chloride content of the fluids was slightly decreased in 4, normal in 6, and slightly increased in 3 of the 13 cases in which this determination was made. The lowest chloride was 666 mg. per 100 cc., the highest 768 mg. The average was 710 mg.

There was no decolorization of the colloidal gold solution by the fluids from 5 cases, and an insignificant change was produced by those from 10. Complete or incomplete decolorization of the solution was produced by the fluid from 1 case, which gave a first-zone curve (5555432100), and by those from 8, which gave mid-zone or end-zone curves.

The Wassermann and Hinton reactions were negative in all fluids.

#### TREATMENT

In our present state of knowledge, treatment is mainly confined to supportive measures. In the recent cases, we have administered large doses of vitamin preparations, particularly vitamin B<sub>1</sub> and the vitamin B complex, which have not had any appreciable effect on the course of the disease.

The possibility of respiratory failure must always be kept in mind, and suction apparatus for the removal of mucus should be available. The pa-

tient should be placed in a respirator as soon as respirations become inadequate, as evidenced by cyanosis or labored respiration. Difficulty in administering intravenous stimulants by the usual method to patients in the respirator has led us to the injection of these drugs into the internal jugular vein. We have found this quite easy to do, since it does not interfere with the respirator and is simpler than using the external jugular vein.

To prevent contractures and to maintain the muscles as well as possible, the legs and arms should be splinted and a cradle used over the bed. When the acute stage has passed, physiotherapy—in the form of massage, heat, passive movements and exercise—is added.

If dysphagia is present, feedings should be restricted to liquid, high-calorie, high-vitamin diets, with gradual institution of semisolid and solid food as the patient's condition warrants.

#### END RESULTS

Eleven of the patients died. This gives a mortality rate of 42 per cent, which is in sharp contrast with the figures given by other authors. However, we found that of the 10 patients studied between 1938 and 1940, 8, or 80 per cent, died, whereas prior to 1937 there were 16 cases with only 3 deaths, or a mortality of 19 per cent. A striking increase in the virulence of the disease is apparent.

Eight of the 15 patients who survived were subsequently examined in follow-up studies; the remaining 7, who were improved at the time of discharge, could not be found. Of the 8, 5 had recovered completely, 1 had slight residual symptoms, and 2 had marked residual symptoms.

Those making a complete recovery did so in an average of fifty-seven weeks, with a variation from six weeks to three years. These patients have been able to resume gainful occupations, and careful neurologic examinations have revealed no abnormal findings. The patient with slight residual symptoms had been unable to walk for sixteen months without aid. After four years, he was able to return to his employment as a salesman. Careful examination of this patient revealed slight foot drop on the left, weakness of both extensor halluc muscles, some atrophy of the left thenar eminence, with minimal weakness of the extensor digitorum muscle on the left. A stocking type of hypesthesia to pinprick and touch persisted to the right ankle. Of the 2 patients with marked residual symptoms, one, in the course of three years, developed a picture suggestive of progressive muscular atrophy and the other, four years after

the illness, showed residual weakness of the left arm and both legs, with atrophy

### PROGNOSIS

In the fatal cases, the age varied from three to seventy-eight years, with an average of thirty-three years, as compared with an average of thirty-four years for the nonfatal cases, hence, age appears to have no effect on the outcome

Our series is too small to be statistically adequate, but it appears that the disease is more virulent in women, since the mortality rate for females was 72 per cent, as compared with 32 per cent for males

Eleven of the 13 patients requiring artificial respiration succumbed. This emphasizes the prognostic gravity of this complication, even though a respirator is used

The presence of an infection prior to the onset of the neuritic symptoms was not of significance, since this was recorded in 50 per cent of the entire group and in 45 per cent of the fatal cases

Loss of cutaneous sensation was found in 45 per cent of the fatal cases, a figure which is approximately the same as that for the entire group 42 per cent

There was nothing to indicate that the presence or absence of abnormalities in the cerebrospinal fluid played a role in the prognosis. There was a pleocytosis in the fluid of 1 of the fatal cases, and the average protein content of the fluids from the patients who recovered was 180 mg, as compared with 130 mg for those who died

### CASE REPORTS

**CASE 7** A 25-year-old Jewish man was admitted on January 24, 1938, with a history of a severe upper respiratory infection 3 weeks earlier. In the interim, he was able to continue in his occupation as a baker. Five or 6 days before admission, he noted pain in his legs, followed by paresthesias in all extremities and weakness that progressed so that by the time of admission he could not walk and could turn over in bed only with difficulty. On the day of admission, difficulty in swallowing solids developed.

The past and family histories were irrelevant. The temperature was 98°F, the pulse 96, and the respirations 18.

The patient was well developed and well nourished and appeared acutely ill. He was unable to swallow solids or to lift his arms or legs from the bed. There was no mental clouding. The face was masklike with a bilateral weakness, more marked on the right. The voice was thick and there was difficulty in raising saliva, which he was unable to swallow. The gag reflex was absent and the palatal movements were weak. There was moderate weakness of the trapezius and sternomastoid muscles. The weakness of the extremities was more marked at the proximal joints than at the distal ones. The trunk muscles were also weak. Sensory examination was negative,

except for a slight diminution of vibratory sense over the ankles. All deep and cutaneous reflexes were absent.

The urine contained a slight trace of albumin and an occasional hyaline cast, the red-cell count was 4,900,000 with a hemoglobin of 98 per cent, and the white-cell count was 7360 with a normal differential count. The blood Hinton reaction was negative. The spinal fluid was under an initial pressure of 90 mm of water. The fluid was clear and colorless, with 2 lymphocytes per cubic millimeter, a protein of 146 mg per 100 cc, a colloidal gold curve of 0000111000 and negative Hinton and Wassermann tests.

While he was in the hospital, the patient's course showed some variation. He became much worse, especially in regard to deglutition on the 1st day of hospitalization, but on the following day, January 25, he was somewhat improved. By January 28 he was again progressing downward and had developed diarrhea and fecal incontinence, the difficulty in raising mucus was more pronounced by January 31. On February 1 he developed paralysis of the diaphragm and was placed in a respirator, but was removed later that day. On February 3, however, he suddenly again developed respiratory paralysis and the pulse became progressively rapid, thready and weak, he became restless, disturbed, anxious, cyanotic and ashen, his pupils dilated, and he expired suddenly.

**CASE 11** A 23-year-old Italian was admitted on August 14, 1935, with a history of pain and weakness in both legs of 17 days' duration, with intermittent numbness and pain in the teeth. There was no preceding infection, but prior to entry the patient had lost weight and had had anorexia and malaise.

The family and past histories were irrelevant.

The temperature was 99°F, the pulse 100, and the respirations 20.

The patient was well developed and well nourished, and appeared to be acutely ill. There were diminished pain, touch and corneal reflexes in the right trigeminal distribution, with weakness of the right pterygoid muscles, complete peripheral facial paralysis on the right, and occasional twitching of the left side of the mouth; in addition, there was slight weakness of the right hand, and marked weakness of both legs. There were numbness and tingling of the fingers and toes, with hypsesthesia to pain and touch and to heat and cold of the glove and stocking type. Muscle tenderness was present in all extremities, and the deep reflexes were absent in the legs and left arm and diminished in the right arm. The plantar reflexes were normal.

Examinations of the urine were negative, the red-cell count was 3,920,000 with a hemoglobin of 71 per cent. Lumbar punctures showed initial pressures of from 110 to 140 mm of water, with normal dynamics. The cerebrospinal fluid was slightly yellow, it contained 44 cells per cubic millimeter and had a protein of 168 mg per 100 cc, a sugar of 53 mg, a chloride of 694 mg and a colloidal gold reaction of 0122332210. Blood Hinton and spinal fluid Hinton and Wassermann reactions were negative.

During hospitalization there was a progressive improvement, except for a slight, short-lived exacerbation early in September. The weakness of both cranial nerve and axial musculature showed considerable improvement under physiotherapy, and on November 22 the patient was discharged. On April 30, 1936, he developed a severe upper respiratory infection, with pain in the legs, and was readmitted. Examination showed residual weakness of the legs with muscular tenderness, slight impairment of po-



sition and vibration sensations and increased knee but diminished ankle jerks. Laboratory study, including lumbar puncture, was entirely negative. On June 2 the patient was discharged. Braces, which he had worn since his first discharge, still had to be applied to his legs.

The patient was last seen on February 2, 1940, in follow-up at our request. He was free of complaints, and stated that he had worn the braces for 14 months and that he was able to return to work as a salesman in August, 1938. Neurologic examination was negative.

#### DIFFERENTIAL DIAGNOSIS

Polyneuritis with facial diplegia or so-called "infectious polyneuritis" is characterized by the relatively acute onset of paralysis or marked weakness of the muscles of the extremities, trunk and face, with or without other cranial-nerve paralyses. The weakness of the extremities differs from that seen in other forms of polyneuritis in that the muscles of the proximal joints are more profoundly affected than those of the distal ones. The development of respiratory difficulty is common. The deep reflexes are lost in the extremities, but the cutaneous sensory loss is rarely severe. The only significant positive finding on laboratory study is an increase in the protein content of the cerebrospinal fluid. The chief differential problems are acute anterior poliomyelitis, encephalomyelitis and peripheral neuritis of other origin. The progressive involvement with a diffuse symmetrical paralysis and the changes in the cerebrospinal fluid are of especial value in the exclusion of poliomyelitis. Comparison of the figures for cells and proteins given above with those of poliomyelitis<sup>10</sup> shows a sharp discrepancy in the number of cells and the protein, when one considers

the duration of illness at the time of puncture. In the differential diagnosis from encephalomyelitis, the chief feature is the peripheral nature of the involvement. The relative absence of pleocytosis, as well as the high protein content, is a further aid. So far as other neuritides are concerned, the picture clinically differs from that of the alcoholic and toxic neuritides in its widespread involvement and particularly in the cranial-nerve involvement.

#### CONCLUSION

Perhaps the most important conclusion obtained from this study of 26 cases of polyneuritis with facial diplegia is that the previously held opinion that the disease always offers a good prognosis is erroneous. The mortality in recent cases has been high, and this increase in virulence is possible evidence for a virus etiology.

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## CARCINOMA OF THE FEMALE BREAST\*

## Interval Report on the Results of Treatment

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THIS is the second report concerning the results of treatment of carcinoma of the breast from the clinic of the Free Hospital for Women.<sup>1</sup> It covers consecutive primary cases admitted to this hospital and its private wing, the Parkway Hospital, from November, 1900, to January, 1935. In each case the diagnosis has been made or confirmed microscopically, with the exception of 9 cases in which the disease was too far advanced to warrant operation. A special attempt has been made to evaluate the use of prophylactic x-radiation, that is, x-rays used either preoperatively or, for the most part, immediately following operation as a precaution against recurrence.

The treatment of choice has been a radical mastectomy, at times supplemented by x-ray therapy. By a radical operation is meant the removal of the whole breast, both pectoral muscles, with the exception of a narrow strip of the pectoralis major along the clavicle, and the axillary contents, including the deep fascia from the axillary vein to the epigastrum and from the sternum to the latissimus dorsi muscle, sparing only the long thoracic and thoracodorsal nerves. The procedure is contraindicated when the disease is known to have spread beyond the axilla; no attempt has been made to remove lymph nodes above the clavicle. It is also contraindicated if the tumor has grown into the chest wall, or if axillary metastases are fixed. It is not attempted if the patient is a really poor operative risk. A simple mastectomy, sometimes under local anesthesia, has often been resorted to in patients who are poor risks. This procedure has also been used as a palliative measure to prevent a sloughing necrotic mass on the chest wall, even though the disease has spread beyond the hope of cure. It is not upsetting, is often a great mental aid to the patient, and, in the opinion of the surgical staff, unless the disease has grown into the chest wall, gives cleaner and, for that reason, better results than x-ray alone.

## GENERAL RESULTS

All cases have been analyzed according to the five-year salvage. No case has been omitted. All patients lost or dead of any cause whatsoever have

been rated dead of cancer. At the end of five years, 138, or 36.7 per cent, of the 376 patients covered in this series were known to be alive. Of those who died, 5 were postoperative deaths, a mortality of 1.3 per cent. Pulmonary embolism, shock, diabetic coma and cerebral hemorrhage each accounted for a death. The fifth patient died while being treated with colloidal lead, which in 1928 was being tried as a therapeutic agent.‡ Before the end of five years, 5 more patients were reported to have died of causes other than carcinoma, namely, cerebral hemorrhage, heart dis-

TABLE 1. *Survival Periods in 376 Cases of Carcinoma of the Breast.*

Total number of cases to January, 1935	376
Total number of patients living at end of 5 years	138 (36.7%)
Of 376 cases	
Untraceable for 5 years	19
Died of cancer before 5 years	209
Died of other causes	10
Of 138 survivors	
Alive with a recurrence less than 10 years	3
Died of cancer less than 10 years	22
Died of other causes less than 10 years	7
Total number of cases to January, 1930	246
Total number of patients living at end of 10 years	41 (16.6%)
Of 246 cases	
Untraceable for 10 years (lost before 5 years, 14, between 5 and 10 years 15)	29
Died of cancer before 10 years	163
Died of other causes before 10 years	13
Of 41 survivors	
Alive with a recurrence less than 15 years	1
Died of cancer less than 15 years	11
Died of other causes less than 15 years	4
Total number of cases to January, 1925	157
Total number of patients living at end of 15 years	14 (8.9%)
Of 157 cases	
Untraceable for 15 years (lost before 5 years, 10, between 5 and 10 years, 6, between 10 and 15 years, 2)	18
Died of cancer before 15 years	114
Died of other causes before 15 years	11
Of the 14 survivors	
Died of cancer (15, 16, 19, and 26 years post-operatively)	4

ease, dissecting aneurysm, arteriosclerosis and monocytic leukemia. Nineteen cases (5.0 per cent) could not be traced.

Of the patients studied ten and fifteen years after admission, 16.6 and 8.9 per cent respectively, were known to be alive (Table 1). The longest postoperative interval was twenty-nine years and

‡This colored patient died of anaphylactic shock or pulmonary embolus one hour and forty five minutes after her first injection of colloidal lead, made according to the specifications of Professor Blair Bell and given twelve days after a radical mastectomy. Five other patients received similar injections of the same preparation on the same day without unusual disturbances.

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nine months. Two other patients were followed for twenty-eight years. The longer follow-ups are interesting, not so much from the percentage of people living, since many were lost or had died of other causes, but because they reaffirm that the five-year interval in breast cancer is useful merely for comparison, since 25 patients died of carcinoma or were living with recurrence between the fifth and tenth postoperative years, 12 between the tenth and fifteenth years, and 4 died of the disease more than fifteen years after treatment. One of the latter patients is noteworthy. Her original tumor was classified as one of low malignancy. Seven and twenty-five years after the first operation, large local recurrences were removed at other hospitals. Nearly twenty-six years after removal of the breast, the patient received radium at this hospital for carcinoma of the endometrium. Obesity and hypertension interdicted a hysterectomy. Death from pulmonary embolus occurred thirty-two days after a radium application and eleven days after the completion of fifteen treatments with x-rays. These treatments had been given without mishap, and the patient had been discharged in satisfactory condition.

Of the 376 patients, 9 were completely inoperable and died within one and a half years of admission.

A radical mastectomy was performed in 284 cases. Metastatic disease was found in the axilla and confirmed on microscopic examination in 159 cases; in 9 others it was unmistakably present from the description of the operation, but the lymph nodes were not sectioned. Of the patients with axillary metastases, 40, or 24.4 per cent, survived for five years; of 116 without axillary involvement, 70, or 60.3 per cent, were alive at the end of this interval.

A simple mastectomy or incomplete procedure was performed on 83 patients: on 38 as a palliative measure and on 45 because most of them were poor operative risks. Of the former, none survived five years, but of the latter, 28, or 62.2 per cent, lived the five-year span, although 10 eventually died of recurrence. These women were for the most part elderly, all but 5 being sixty years of age or more and one third being over seventy. In selected cases, simple mastectomy is of great value, but it should never supplant radical mastectomy as a routine procedure since one cannot tell whether metastatic nodules are present in the axilla until it is dissected.

One has the impression that in recent years the prognosis for carcinoma of the breast is better than formerly. Therefore, the cases have been

divided into groups, one including those seen from 1900 to 1919, inclusive, and three five-year groups—1920–1924, 1925–1929 and 1930–1934. For this purpose, corrected figures have been used. With the exception of patients dying postoperatively, since these might be considered to have died as a result of cancer, those dead of causes other than carcinoma before the end of the five-year interval have been omitted as inconclusive. Lost cases have not been included because a more careful follow-up by the social-service workers in recent years results in fewer of them, and this in itself might account for an improved figure. Thus the five-year salvage has increased from 31 to 38 to 39 to 44 per cent. Moreover, the 1930–1934 group without corrections shows better results in every respect than the large group. Of the patients in the 1930–1934 group subjected to a radical mastectomy, 67 per cent of those with early lesions lived five years, as did 29 per cent of those with lymph-node involvement. If corrected figures are used again in both the 1930–1934 group and the whole series, a comparison shows a five-year salvage of 71 per cent for the early cases in the former and 62 per cent in the latter; for the advanced cases, 31 per cent in the former and 26 per cent in the latter.

Only two obvious changes have taken place that might account for this improvement: propaganda to induce the patients to enter the hospital sooner and more frequent prophylactic x-radiation.

Early diagnosis is obviously of the greatest importance. Patients with no axillary metastases have a far better prognosis—at least twice as good—than those in whom positive nodes are found. Thirteen per cent more patients reported in less than three months from the time they had first noted trouble in the 1930–1934 group than in the 1920–1924 one. Unfortunately, an appalling number still have symptoms for a year or more before coming in for treatment. This was true of approximately one third of the 1930–1934 group. All too often metastases are found in the axilla at operation when the patient has noted a tumor for two weeks or less, and when even the surgeon does not believe that a cancer will be found when the lesion is biopsied.

#### PROPHYLACTIC X-RADIATION

An evaluation of the use of prophylactic x-radiation has been attempted. To do this, as nearly identical cases as possible must be compared. Therefore, only cases submitted to radical mastectomy have been considered, and these have been divided according to whether or not the dis-

case was found in the axillary nodes, and according to the microscopic degree of malignancy\*.

Patients were first referred for prophylactic x radiation from this hospital in 1918. In the beginning it was employed in a somewhat hit-or-miss fashion at the discretion of the surgeon, but from 1929 on it was used almost routinely.† Although the dosage varied widely in the early days, the majority of patients received between 2000 and 3000 r postoperatively, in doses of 250 to 300 r every third or fourth week until it was decided that the proper amount had been reached. In 1929 the method of irradiation changed. The majority of patients received a total of 4800 r. Treatments totaling 1600 r were given usually within 1 week, 400 r at a sitting, two treatments to the front and two to the back of the chest and lower neck on the affected side. Except in 16 patients in whom the first series was given immediately after operation, the technique was to give the first series of 1600 r postoperatively as soon as the skin

mastectomies and have been divided into advanced or early cases, depending on whether axillary metastases were present. They have further been divided into groups according to the degree of malignancy.

Except for the advanced cases in Groups I and III, the percentages were better when x ray treatment was given, but only significantly so in the early cases of Group III. The fact that there was twice as large a salvage of early cases in the high malignancy group when x radiation was given does not appear to be a coincidence, and argues against the idea that it is better to withhold x-ray therapy when no metastatic axillary nodes are found. Further, the failure of x ray treatment to improve the results in the advanced Group III cases supports the opinion that it is inadvisable to do an incomplete operation with the hope that irradiation will take care of any cancer that may be left behind.

Table 3 demonstrates the amount of prophylactic x radiation used in the preceding cases.

If all the radical mastectomies are grouped without reference to the degree of malignancy or dosage, there is a decided advantage for those receiving radiation. Thus, of the patients without

TABLE 2 Comparison of Patients Treated with Those not Treated by X Radiation

	X RAY TREATMENT GIVEN			NO X RAY TREATMENT GIVEN		
	NO OF CASES	5 YEAR SURVIVAL	PER CENT	NO OF CASES	5 YEAR SURVIVAL	PER CENT
Group I (low malignancy) 10 cases						
Axillary nodes not involved	3	3	100	5	4	80
Axillary nodes involved	1	0	0	1	0	0
Group II (medium malignancy) 152 cases						
Axillary nodes not involved	30	18	60	41	24	59
Axillary nodes involved	35	14	40	47	15	33
Group III (high malignancy) 123 cases						
Axillary nodes not involved	20	14	70	17	6	35
Axillary nodes involved	30	4	13	54	7	13

had healed and to repeat it at the end of two or three months and again at the end of a year‡.

Table 2 is a comparison of those patients who received prophylactic x radiation, regardless of dose, with those who had none. All had radical

TABLE 3 X Ray Dosage in Patients also Treated by Radical Mastectomy

DOSAGE	AXILLARY NODES NOT INVOLVED			AXILLARY NODES INVOLVED		
	NO OF CASES	5 YEAR SURVIVAL	PER CENT	NO OF CASES	5 YEAR SURVIVAL	PER CENT
300 r	0			3	1	33
600-900 r	3	1	33	4	0	0
1000-1500 r	5	3	60	1	1	100
1600-2000 r	8	3	38	10	1	10
2000-4000 r	29	19	66	37	7	28
5000 r or more	4	2	50	9	4	44
Uncertain amount	4	3	75	5	2	40

axillary involvement, 66 per cent (corrected, 69 per cent) of those radiated were alive, as contrasted with 54 per cent (corrected 58 per cent) for those without radiation, and for the patients with advanced disease 27 per cent (corrected 29 per cent) of those radiated were alive as compared with 22 per cent (corrected 24 per cent) for those not so treated, however, equally good end results have been obtained by others without x radiation.<sup>4</sup> No serious complications have been noted from x radiation in the dosage used.

#### X-RADIATION FOR RECURRENCES

Twenty-one patients who previously had not been given x rays prophylactically were so treated for recurrent nodules. The dosage varied according to the tolerance of the patient and the reaction of the tumor. The average length of life following the institution of this form of therapy was

\*Greenough's<sup>1</sup> modification of Broder's classification for malignancy was followed as closely as possible. Of 283 patients who had a radical mastectomy 10 were in Group I or showed low malignancy, 152 in Group II and 123 in Group III. In the low malignancy group 70 per cent were known to be living at the end of five years. Of the cases in Groups II and III, 47 and 26 per cent respectively survived. As is to be expected the higher the degree of malignancy the worse the prognosis.

†Factors: target skin distance 50 cm., filter copper 0.5 mm., aluminum 1.0 mm., kV. 100, 20 by 30 cm. Before 1929 the x ray therapy was generously given by Dr. L. E. Morrison from 1929 on treatments have been given by Dr. John Meclen whose cooperation is gratefully acknowledged.

‡Since the fall of 1937 it has been customary to give all irradiation to tolerance in one long series of treatments.

two years. Only one patient survived five years, and she eventually died of cancer. In 9, or a little more than a third of the cases, the disease disappeared at least temporarily; hence, this form of therapy seems to hold the disease in check or greatly to improve the health of the patient in about 1 out of 3 cases.

RADIUM

Radium has been used as supplementary treatment in 15 of the reported cases. Well screened, it has been placed against local areas of disease. In all but one case, when it was applied to the axilla at operation, it has been used on recurrent nodules. It causes the disease to regress or temporarily disappear, but except for less systemic reaction, it has no advantage over deep x-ray therapy and does not cover so large a field.

AGE AS A PROGNOSTIC FACTOR

The age of the patient may be of interest from a prognostic standpoint. The youngest was twenty-four years old on admission, and the oldest eighty-one. Forty-three were under forty; 5 were less than thirty. These facts remind one that a tumor of the breast must not be viewed complacently because the patient is young, although the disease is predominantly one of older people. The largest five-year group (62) presented themselves be-

type. Of the 5 patients, 3 had tumors of a high degree of malignancy, and that of the survivor was of medium malignancy, which confirms this suggestion. However, if all the cases are divided into twenty-year groups, the percentage of five-year salvage for all admissions regardless of treatment or extent of the disease is 40 per cent for 43 cases twenty-four to thirty-nine years of age, 30 per cent for 201 cases forty to fifty-nine, and 43 per cent for 127 cases sixty to eighty-one. It will be noted that the poorest five-year salvage was in the middle age group. This may be partly explained by the degree of malignancy, for if the same age groups are analyzed, it is found that, in the younger group, 4 (9 per cent) were in Grade I, 18 (41 per cent) in Grade II, and 18 (41 per cent) in Grade III, and 3 were unclassified.<sup>\*</sup> In the middle age group, 5 (2 per cent) were in Grade I, 104 (52 per cent) in Grade II, and 88 (44 per cent) in Grade III; 4 were not graded. In the older age group, 7 (5.5 per cent) were in Grade I, 65 (51 per cent) in Grade II, and 50 (39 per cent) in Grade III; 5 were not classified. Among these cases, the middle age group had a slightly higher percentage of highly malignant tumors, but it is noteworthy that there was a very even distribution of tumors of high and low malignancy in each age group.

The more immature tumors, however, are malignant because they metastasize early, not because they are rapidly growing in situ. Thus, of the cases subjected to a radical mastectomy, diseased axillary nodes were found in 20 per cent of Grade I, 53 per cent of Grade II and 69 per cent of Grade III.

SUMMARY AND CONCLUSIONS

Three hundred and seventy-six cases of carcinoma of the breast have been analyzed. Thirty-six and seven-tenths per cent of all patients admitted to the hospital were known to be alive five years after treatment.

There is no criterion for absolute cure for cancer of the breast, since many patients died of carcinoma fifteen or more years postoperatively.

A radical mastectomy was performed in 284 cases. Of the patients without axillary metastases, 60 per cent were living at the end of five years, as were 24 per cent of those with axillary involvement. Prognosis has improved with the years; thus, the 1930-1934 group shows a salvage of 67 per cent for the early cases subjected to radical mastectomy, and 29 per cent for those with axillary involvement. If corrected figures are used, the percentages become 71 and 31, respectively.

A simple mastectomy was of value in poor op-

<sup>\*</sup>Twelve cases were unclassified, 9 because they were inoperable and 3 because the slides were not available.

TABLE 4. Age Distribution.

AGE	No. of Cases
37.	
25-39	43
25-29	5
30-34	11
35-39	27
40-59	201
40-44	39
45-49	62
50-54	55
55-59	45
60 and over	127
60-64	58
65-69	34
70-74	21
75-79	10
80 and over	4
Unknown	5

tween the years of forty-five and forty-nine, inclusive, but each succeeding group to the age of sixty-five was nearly as large; 35 patients were over seventy years of age (Table 4).

It has been held that the younger the patient, the poorer the prognosis in carcinoma of the breast. Of the 5 patients under thirty years of age, only 1 was well at the end of five years. It has been suggested<sup>3</sup> that younger women do badly because the tumor is apter to be highly malignant, but that if the tumor is of low malignancy they do as well as older patients with tumors of the same

erative risks, there being a 62 per cent five year salvage for selected patients in whom there was no obvious metastasis at operation. This procedure should be used only in really bad operative risks, however, since it is impossible to rule out axillary metastases preoperatively.

The total operative mortality was 1.3 per cent.

The prognosis for carcinoma of the breast is improving. A combination primarily of earlier admissions and secondarily of prophylactic x-radiation is considered to be the reason. The cases in this series showed better results when radiation was given than when it was withheld.

Prophylactic x-radiation is thought to be of advantage, particularly in patients with tumors of high malignancy with no apparent axillary involvement. It seems wiser to use it routinely than on advanced cases only.

X-ray or radium therapy retards or causes the growth to disappear in about one third of the patients with recurrent disease. It seldom effects a five-year cure.

Cancer of the breast is not infrequent in young women, but is primarily a disease of elderly people.

Although the degree of malignancy is of significance in the prognosis of cancer of the breast, since highly malignant tumors tend to metastasize earlier, it is the extent of the disease at operation that is the most significant factor.

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### THE LAW AND MENTAL DISEASE\*

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THE generous invitation to address you who are in fields of specialization in the medical realm, coupled with an urge that the subject matter have reference to the law and insanity, is responsible for my appearance before you today. To dwell at length on a matter of such great importance, and about which volumes have been written, is obviously an utter impossibility. In the comparatively short time allotted, therefore, only cursory observations can be presented for your reflection.

This assembly is composed of men and women of scientific bent and training. Science savors of independence in thought and action. It has been individual exercise of this virtue that has produced so many humanitarian results. Despite great obstacles and seemingly insurmountable difficulties, even including persecution, individualistic genius, courage and perseverance have brought victory. Apropos of this suggestion, it seems fitting to make reference to the life of a man to whom finally was given the credit for a great contribution, not only to the medical profession but to the entire world. I refer to Dr. W. T. G. Morton and the anesthetic, ether.

Just as ether has properly taken its place in the realm of blessings, other great and material factors have contributed to the advancement of man. For at least one of these factors, it is my assumption that many of those here gathered have an

affectionate regard. It is a part of their daily life; it is their profession; it is their pursuit; it is their happiness. They are the medical examiners, whose main duty it is to observe and examine and to determine the cause of death.

We who love America abhor regimentation of thought and action resulting from dictatorship. It is natural that we do, for our very beings are part and parcel of the greatest fountain of government on earth, the Constitution of the United States. From it our rights flow. They are termed constitutional rights or privileges. They are not mythical prerogatives; they are fundamental and realistic. The citizen of today has been awakened from the state of indifference and is appraising more definitely and truly the national life. Governments operated as a machine concerning the destiny of which the voice of the individual has no control, individuals or coteries of persons who set up their own style of government for the present and for the sake of expediency, those who seek to conquer and who are imbued with the false doctrine that "might makes right," have at last made an impression, and it is to be hoped, an indelible one, that one is fortunate to live in "the land of the free," where democracy really means freedom under the law and where the "consent of the governed" is paramount.

The Constitution of the United States is not a paradise for the legal profession. It is not the *sanctum sanctorum* for judges and lawyers. It is the life of all Americans. Permit me to read what

\*Presented at the annual meeting of the Massachusetts Medico-Legal Society Boston May 21, 1940.  
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many Americans have probably not yet read, the preamble to the Constitution: "We, the people of the United States, in order to form a more perfect union, establish justice, insure domestic tranquility, provide for the common defense, promote the general welfare, and secure the blessings of liberty to ourselves and our posterity, do ordain and establish this Constitution for the United States of America."

The words, "secure the blessings of liberty to ourselves and our posterity," are all-significant. They refer to you and me; they mean the medical and legal professions; they are synonymous with the doctrine of the Golden Rule. In short, we have enjoyed the right to live in our chosen sphere protected by laws passed by Congress,—the legislative body,—acting only by virtue of the authority contained in the provisions of the Constitution.

So it is in Massachusetts. We have a state constitution second to none. By virtue of its provisions, the legislature from time to time has passed various laws for our government. Of course, laws passed by the state legislature cannot be inconsistent with or antagonistic to the provisions of the Constitution of the United States or laws passed by Congress.

Massachusetts has led the way to a great extent in the passage of humanitarian laws. Labor and health laws predominate. Other states in the Union have from time to time emulated our example. The State of New York—so I was told by a late member of this society, Dr. George Burgess Magrath—through its designated representatives sought advice when the coroner's system was to be abandoned. The medical-examiner method under our law appealed to those in New York State who were experts in dealing with sudden and violent death and its causes. It is my understanding that a study of the system in Massachusetts materially helped in the molding of the new and present one in New York State.

It is my humble judgment that the manner of selecting the medical examiners in Massachusetts is the main reason for success. This is my fourteenth year in the office of district attorney. There are eleven medical examiners, besides assistants, in the district that I represent, comprising four counties. It has been my duty, under the law, to authorize them to perform autopsies. Therefore, I have been afforded an opportunity to appraise them, because of my almost continual association with them in their work. They have proved overwhelmingly a faithful and capable body of public servants.

Section 1 of Chapter 38 of the General Laws of Massachusetts provides, in part, that "the governor, with the advice and consent of the council,

shall appoint for terms of seven years able and discreet men, learned in the science of medicine, as medical examiners in and for their respective counties, and as associate medical examiners in and for their respective districts . . . , otherwise in and for their respective counties. . . ."

You can readily appreciate that the responsibility by law is vested in the governor of the Commonwealth to appoint, and that confirmation is the prerogative of the executive council.

The judges of all the courts of the Commonwealth are similarly appointed and confirmed. They enjoy a life tenure of office.

The system of judicial appointments and tenure of office in Massachusetts has been generally commended. It has not been changed, although at times it has been assailed. Therefore, it seems but fair to contend that it has worked for the common good; and this is due to the fact that the governor and the council have followed the admonition of the statute and kept faith with its provisions. So it has been with the appointment of medical examiners.

As the law provides for the care and supervision of bodies and the determination of the cause of death in the interest of justice, so the law makes provision for the living in many ways. Particularly, does the law provide through various channels and agencies for human beings who are mentally sick. It provides for the treatment of all insane, feeble-minded and epileptic persons, and all persons addicted to the intemperate use of narcotics or stimulants. Further provision is made that no county, city or town shall establish or maintain any institution for the care, control and treatment of insane, feeble-minded or epileptic persons, or to persons addicted to the intemperate use of narcotics or stimulants, or be liable for the board, care, treatment or act of any person who shall be committed into or received by any state hospital.

The Department of Mental Health, the executive of which is the commissioner of mental health, has general supervision of all public and private institutions for insane, feeble-minded or epileptic persons, or for persons addicted to the intemperate use of narcotics or stimulants, and has charge of all persons whose care is vested in the Commonwealth by law, and supervision of all other persons received into any of these institutions.

The department takes cognizance of all matters affecting the mental health of the citizens of the Commonwealth, and makes investigation of all causes and conditions that tend to jeopardize mental health, and the causes of mental disease, feeble-mindedness and epilepsy, and the effects of employment, conditions and circumstances on men-

tal health, including the effect thereon of the use of drugs, liquors and stimulants

The commissioner administers the laws relative to persons in institutions under the general supervision of the department and prepares rules and regulations for the consideration of the department

The members of the department act as commissioners of insanity, with power to investigate the question of the sanity and condition of any person who is an inmate of any institution for the insane, public or private, or restrained of his liberty by reason of alleged insanity at any place within the Commonwealth, and discharge any such person, if in their opinion he is not insane or can be cared for after such discharge without danger to others and with benefit to himself.

There are a number of state institutions under the supervision of the Department of Mental Health, including the Worcester State Hospital, Taunton State Hospital, Northampton State Hospital, Danvers State Hospital, Grafton State Hospital, Westboro State Hospital, Foxboro State Hospital, Medfield State Hospital, Monson State Hospital, Gardner State Hospital, Wrentham State School, Boston State Hospital, Walter E. Fernald State School, Boston Psychopathic Hospital, Belchertown State School and Metropolitan State Hospital. The Bridgewater State Hospital for the criminally insane is under the jurisdiction of the Department of Correction and under the control of the superintendent of the State Farm at Bridgewater. The general interest and affairs of each state hospital are managed by trustees, who, with the approval of the department, appoint and may remove a superintendent, who shall be a physician and shall reside at the hospital.

A justice of the Superior Court in any county, either of the judges of probate for Suffolk County, the judge of probate for Nantucket County and a justice or special justice of a district court, except the municipal court of the City of Boston, within his county may commit to any institution for the insane, generally speaking.

It is provided that no person shall be committed to any institution for the insane unless there has been filed with a qualified judge a certificate of the insanity of such person by two properly qualified physicians, or without an order therefor, signed by the judge stating that he finds that the person committed is insane and is a proper subject for treatment in a hospital for the insane. No physician shall make a certificate for insanity unless he makes oath that he is a graduate of a legally chartered medical school or college, that he has been in the actual practice of medicine for three years since his graduation and for three

years preceding the making of said oath, and that he is properly registered as a physician, nor unless his standing, character and professional knowledge of insanity are satisfactory to the judge. A physician who makes such certificate shall have examined the alleged insane person within five days of his signing and making oath to the certificate, shall state therein that in his opinion such a person is insane and a proper subject for treatment in a hospital for the insane, and shall present the facts on which his opinion is based. The judge may, in his discretion, issue a warrant to the sheriff or his deputy, directing him to summon a jury of six men to hear and determine whether the alleged insane person is insane.

If two physicians, qualified as heretofore stated, find a person to be in such mental condition that his commitment to an institution for the insane is necessary for his proper care or observation, he may be committed by a judge to a state hospital for a period of thirty-five days pending the determination of his sanity. Within thirty days after such commitment the superintendent of the institution to which the person has been committed shall discharge him if he is not insane, and shall notify the judge who committed him, if he is insane, the superintendent shall report the patient's mental condition to the judge with the recommendation that he be committed as an insane person, or discharged to the care of his guardian, relatives or friends if he is harmless and can properly be cared for by them. Within the thirty-five-day period, the judge may authorize a discharge as aforesaid, or he may commit the patient to any institution for the insane as an insane person, if, in his opinion, such commitment is necessary. If the judge considers additional medical testimony of the mental condition of the alleged insane person to be desirable, he may appoint a physician to examine and report thereon.

The authorities in state hospitals are authorized by law to receive and detain therein as a boarder and patient any person who is desirous of submitting himself to treatment who makes written application therefor, and who is mentally competent to make the application; and any such person who desires to submit himself for treatment may make the written application. No such person shall be detained more than three days after having given written notice of his intention or desire to leave the institution.

America is indebted to England for many contributions to its institutions of government. Magna Charta is a famous English document that was signed by King John on June 15, 1215, at a meadow, called Runnymede, on the Thames near Windsor. The king had failed to live up to cer-



tain agreements with his barons, and they threatened to make war on him unless he conceded certain rights to them by a sealed charter. He finally yielded. It contained sixty-three articles setting forth the rights and privileges of each class of citizen and specified the power that the king might assume.

Magna Charta corresponds in a rough way to our constitution. One of the most important clauses, known in history as the thirty-ninth article, declares that no free man shall be taken or imprisoned or outlawed or banished except by the lawful judgment of his peers or the law of the land. This is the basis of the jury.

We are also indebted to England for the writ of habeas corpus. The English colonists in America brought with them this priceless privilege as part of their common-law inheritance. When application is made by an attorney or any friend of the prisoner, the latter is brought into court so that the cause of his detention may be inquired into. The writ is addressed to the sheriff, marshal or other officer having the prisoner in custody. The judge inquires into the charge on which the prisoner is held, and issues an order sending him back to jail, admitting him to bail, or setting him free, as may seem proper. The writ is intended to prevent imprisonment on false or malicious charges. It is incorporated in the Constitution of the United States, which provides that the privileges of the writ shall not be suspended unless, in case of actual rebellion and invasion, the public safety may require it. The necessity of a provision like that of the habeas corpus may be understood the more readily when it is recalled that in France prisoners of state were confined in the Bastille for years or even for life. Their friends had no possible way of bringing them into court to inquire into the causes of their detention, however unjust.

The Constitution of Massachusetts provides that "the privilege and benefit of the writ of habeas corpus shall be enjoyed in this commonwealth in the most free, easy, cheap, expeditious and ample manner." In connection therewith, this remedy is commonly used in criminal proceedings, but specific provision is also made for its use in connection with insane persons, or persons alleged to be sane, whose detention or incarceration is contended to be improper by friends or interested parties.

In justice to those who have charge and supervision of the insane, as well as to the Commonwealth as an entity, I think that it may be truthfully stated that resort to the use of habeas corpus in behalf of patients in state hospitals is a rarity. It is a pleasure for me to testify that in my entire

experience, stretching over a period of approximately fourteen years, no such matter has been called to my attention officially. Furthermore, despite unfortunate happenings that have occasionally occurred in one part of the Commonwealth, not a single complaint has ever come to me for official action. It seems to me that this is another favorable commentary on the laws affecting those who are mentally sick, as well as the personnel of the Department of Mental Health, who administer the said laws.

An outstanding and conspicuously humane piece of legislation became a part of the General Laws of Massachusetts through the efforts of one of the great men in the field of psychiatry in our time. I refer to Dr. L. Vernon Briggs. In my opinion, — and my experience has been with thousands of cases, including many matters of murder, — Dr. Briggs has unselfishly and unwittingly built a monument for himself by the service that he rendered to the citizenry of this commonwealth when in the year of 1921 there was placed on the statute book a law making certain mental examinations mandatory.

Section 100A of Chapter 123 of the General Laws of Massachusetts contains the following provisions:

Whenever a person is indicted by a grand jury for a capital offense or whenever a person, who is known to have been indicted for any other offense more than once or to have been previously convicted of a felony, is indicted by a grand jury or bound over for trial in the superior court, the clerk of the court in which the indictment is returned, or the clerk of the district court or the trial justice, as the case may be, shall give notice to the department of mental diseases, and the department shall cause such person to be examined with a view to determine his mental condition and the existence of any mental disease or defect which would affect his criminal responsibility. Whenever the probation officer of such court has in his possession or whenever the inquiry which he is required to make by section eighty-five of chapter two hundred and seventy-six discloses facts which if known to the clerk would require notice as aforesaid, such probation officer shall forthwith communicate the same to the clerk who shall thereupon give such notice unless already given. The department shall file a report of its investigation with the clerk of the court in which the trial is to be held, and the report shall be accessible to the court, the probation officer thereof, the district attorney and to the attorney for the accused. In the event of failure by the clerk of a district court or the trial justice to give notice to the department as aforesaid, the same shall be given by the clerk of the superior court after entry of a case in said court. Upon giving the notice required by this section the clerk of a court or the trial justice shall so certify on the papers. The physician making such examination shall, upon certification by the department, receive the same fees and traveling expenses as provided in section seventy-three for the examination of persons committed

to institutions and such fees and expenses shall be paid in the same manner as provided in section seventy-four for the payment of commitment expenses. Any clerk of court or trial justice who wilfully neglects to perform any duty imposed upon him by this section shall be punished by a fine of not more than fifty dollars.

This law means that when a person has been before any district or municipal court in the Commonwealth and has been found probably guilty of the crime of murder, and whose case is bound over for the consideration of a grand jury because of lack of final jurisdiction in the lower court, if the grand jury indicts him for murder, it then becomes the bounden duty under law of the clerk of the Superior Court to notify the Department of Mental Health, which was formerly known as the Department of Mental Diseases. Then two psychiatrists, under the direction of the commissioner, make a mental examination of the prisoner. They also arrange with social workers to get the background of the prisoner and his family and relatives, and they make a written report, which is filed by them in the office of the clerk of court for the county where the prisoner is situated and the charge is pending.

The same procedure prevails when a presentation is made in connection with a charge of murder to a grand jury and an indictment against the defendant results. It also prevails when a person has been indicted by a grand jury for any other offense more than once, or has been previously convicted of a felony and is indicted by a grand jury, or is bound over for trial in the Superior Court.

It may be proper for me to suggest at this time that crimes are divided into three classifications: treason, felonies and misdemeanors. Treason is levying war against the Commonwealth or giving aid or comfort to enemies, and is punished by life imprisonment. A crime punishable by death or imprisonment in the state prison is a felony. All other crimes are misdemeanors.

Although it has been the duty of the clerks of the district courts in my district to report cases to the Department of Mental Health when examinations are required, generally I have arranged for a member of my staff to keep in constant touch with the police officials in the various cities and towns and masters of the several jails for the purpose of ascertaining the background of those incarcerated or those on bail awaiting grand-jury action, to determine the necessity of mental examinations. As examinations have been found necessary, communications requesting that they be made have been sent direct from my office to the commissioner of mental health.

Co-operation between the commissioner and

those designated by him to make examinations has been so complete that not only have taxpayers been saved money and the necessity of many prospective trials but the law-enforcement officials as well as the judges have been so fortified with the history and background of the defendants, in addition to the expert opinions of the psychiatrists who examined them, that the constitutional rights of individuals have been safeguarded so far as has been humanly possible, and the ends of justice well served.

This law has done more than any other to make certain that the person charged with a crime in keeping with the provision shall not go to a prison or jail if he is insane or mentally deficient, but rather to a proper institution for treatment.

The examination is made, and opinions given by specialists in mental diseases who are reputable and who are paid a very nominal sum for their services. Their opinions are not high priced ones, nor are they bought and paid for by either the defense or the Commonwealth in competitive manner. There is no incentive for deceit or color. Both sides of any controversy receive the benefit of unadorned medical facts, and as properly as can be, judgment is then predicated thereon.

If this law, or one similar to it, had been passed by a legislature in another great state not far distant from us, I am quite sure that a travesty on justice would have been precluded. It must be true that both the defendants and the states in many other jurisdictions have been irreparably damaged and unjustly treated by the absence of such a legal provision.

It is my hope that in the early future a provision may be incorporated in Section 100 A giving to the authorities a similar jurisdiction over misdemeanors. I believe that people who commit a series of misdemeanors are many times suffering from some mental disturbance or weakness. Because the law does not make mandatory examinations in connection with misdemeanors, miscarriages of justice must on occasions result. To be sure, whenever a question is raised about the sanity or mental status of a person, the court has full power to order an examination, even in the case of a misdemeanor. Likewise, whenever I have wondered about the advisability of a mental examination, the defendant has been given the benefit of the doubt and an examination has been provided. In short, when examinations are made mandatory by law, defendants get the benefit as a matter of routine; but where there is no mandate, justice is often dependent on the exercise of discretion.

I shall mention one more matter that is of vital importance in the realm of law having to do with mental disease. It is referred to as criminal

responsibility. Criminal responsibility means liability to legal punishment. The law assumes that every person, except those in certain exempted classes, possesses the ordinary human faculties—power to choose between right and wrong and to do or refrain from doing what the law commands. The criminal law sets up certain standards of human conduct, and expects conformity therewith. As Justice Oliver Wendell Holmes, Jr.,<sup>1</sup> has said, speaking of these standards of conduct:

They do not merely require that every man should get as near as he can to the best conduct possible for him. They require him at his own peril to come up to a certain height. They take no account of incapacities, unless the weakness is so marked as to fall into well-known exceptions, such as infancy or madness. They assume that every man is as able as every other to behave as they command. If they fall on any one class harder than on another, it is on the weakest. For it is precisely to those who are most likely to err by temperament, ignorance, or folly, that the threats of the law are most dangerous.

At common law, and to a great extent the common law of England has been our heritage, a child under the age of seven years is conclusively presumed incapable of entertaining criminal intent and cannot commit a crime. Between the ages of seven and fourteen the child is presumed to be incapable, but the presumption may be rebutted. After the age of fourteen, he is presumed to have sufficient capacity, and must affirmatively show the contrary.

The ground of an infant's exemption from criminal responsibility for his acts is the want of sufficient mental capacity to entertain the criminal intent that is an essential element of every crime. When a child has reached the age of fourteen, he is presumed capable of committing crime; and to escape responsibility, he must affirmatively show want of capacity. In earlier years these rules were so harshly applied that in England a boy of ten years, who, after killing a little girl, hid her body, was held criminally liable because the circumstances were judged to show a responsible discretion; and a boy of eight years was hanged for arson. In this country, a boy of twelve has been hanged for murder.

Generally speaking, the common-law rules regarding the criminal responsibility of children have been re-enacted in the statutes. In a few states the age of incapacity has been raised by statutes, and in some the age at which presumption of capacity begins has been lowered.

Since the beginning of the twentieth century a new body of law, although not designed to supersede the criminal law on the subject, has had the practical effect of almost completely dispos-

ing the criminal courts of jurisdiction of crime committed by infants. In practically every state, laws have been passed creating juvenile courts, defining juvenile delinquency, providing administrative procedures for determining delinquencies, and for the care, treatment and discipline of delinquent children. This new development has resulted from an unwillingness to apply to children the arbitrary standards of conduct set up by the criminal law or to require of them the same conformity that is required of adults. Its effect is to extend greatly the idea of incapacity of children to commit crime, which the common law has always known. In this commonwealth, I recall the case of Jesse H. Pomeroy, who, a boy of fourteen years and five months at the time of the offense, was tried on an indictment of murder of Horace R. Millen, a child four years old, committed at Boston on April 22, 1874. The jury returned a verdict of guilty of murder in the first degree.

As in cases concerning infants and liability for crime, so in matters having to do with alleged insane persons, criminal responsibility must be determined. In the case of *Commonwealth vs. Abner Rogers, Jr.*,<sup>2</sup> Chief Justice Shaw of the Supreme Judicial Court said:

In order to constitute a crime, a person must have intelligence and capacity enough to have a criminal intent and purpose; and if his reason and mental powers are either so deficient that he has no will, conscience or controlling mental power, or if, through the overwhelming violence of mental disease, his intellectual power is for the time obliterated, he is not a responsible moral agent, and is not responsible for criminal acts.

But these are extremes easily distinguished and not to be mistaken. The difficulty lies between these extremes, in the cases of partial insanity, where the mind may be clouded and weakened, but not incapable of remembering, reasoning and judging, or so perverted by insane delusion, as to act under false impressions and influences. In these cases, the rule of law, as we understand it, is this: a man is not to be excused from responsibility, if he has capacity and reason sufficient to enable him to distinguish between right and wrong, as to the particular act he is then doing; a knowledge and consciousness that the act he is doing is wrong and criminal, and will subject him to punishment. In order to be responsible, he must have sufficient power or memory to recollect the relation in which he stands to others and in which others stand to him; that the act he is doing is contrary to the plain dictates of justice and right, injurious to others, and a violation of the dictates of duty.

The matter of criminal responsibility is left for determination by the jury that hears the particular case. Expert opinion may be given as to the state of mind of the defendant at the time an alleged criminal act was committed. Even the family

history and mental condition both before and after the act may be fully inquired into and introduced as evidence. But the question is not to be finally settled by medical science or by legal definition from the bench, although each may be of material assistance to a jury. It is the duty of the judge to state clearly and sufficiently what the jury must decide by a careful discrimination between the law and the facts that are founded on the evidence. The defendant, even if abnormally deficient in will power and of retarded mental development, can be found to be fully conscious of the criminal character and the consequences of his act. It is also a pure question of fact for the jury to decide whether the defendant is so mentally diseased that he felt impelled to act by a power that overcame his reason and judgment and was irresistible. In the final analysis, however, the jury is legally obliged to determine the defendant's responsibility by ascertaining his state of mind at the time of the commission of the act.

In the case of *Commonwealth vs. Cooper*,<sup>1</sup> the defendant was convicted of the crime of murder in the first degree by a jury. The case was taken by the defendant to the Supreme Judicial Court for a final determination on questions of law. The defendant had asked the judge in the trial court to tell the jury that if the defendant had a mental disorder called "constitutional inferiority," and if the jury found that such a disorder carried with it a diminished degree of responsibility for the act, he could not be found guilty of murder in the first degree. The judge refused to give the requested ruling. The Supreme Judicial Court sustained the trial judge's position, commenting that from the evidence—even though the consensus of the alienists, based on the defendant's family history and their examinations, classified him as constitutionally defective, or possessed of weak and diminished will power and self-control—they were not agreed that he lacked sufficient capacity to distinguish between right and wrong.

Quoting again from the case of *Commonwealth vs. Rogers*, the working rule for the guidance of the jury is summed up in the following words:

If then it is proved, to the satisfaction of the jury, that the mind of the accused was in a diseased and unsound state, the question will be, whether the disease existed to so high a degree, that for the time being it overwhelmed the reason, conscience and judgment and whether the prisoner, in committing the homicide acted from an irresistible and uncontrollable impulse. If so, then the act was not the act of a voluntary agent, but the involuntary act of the body without the concurrence of a mind directing it.

In a comparatively recent case, *Commonwealth vs. Charles Trippi*,<sup>4</sup> which involved a murder and in which the jury returned a verdict of first degree on January 23, 1929, the defendant, twenty-two years of age, was serving a sentence of fifteen to eighteen years in a Massachusetts state prison. Armed with a loaded revolver and thirty or forty extra cartridges, he made an attempt to escape from the prison, during which he shot and killed Frederick Pfluger, a guard of the institution. Certain evidence was offered by counsel for the defendant to establish that the latter's mental age was about thirteen years, as determined by psychometric tests in which event it was contended that the judge should instruct the jury that he was presumed to be incapable of forming a criminal intent. The judge ruled as follows: "I now rule that the showing, if it can be shown, that the defendant was mentally thirteen years of age, as established by the psychometric tests, does not entitle him to the benefit of the presumption claimed by counsel. Having made that ruling, I exclude this evidence on that ground." The Supreme Judicial Court upheld the ruling of the trial judge and said in part:

Criminal responsibility does not depend upon the mental age of the defendant nor upon the question whether the mind of the prisoner is above or below that of the ideal or of the average or of the normal man, but upon the question, whether the defendant knows the difference between right and wrong, can understand the relation which he bears to others and which others bear to him and has knowledge of the nature of his act so as to be able to perceive its true character and consequences to himself and to others.

I have purposely dwelt at length on the matter of criminal responsibility because my experience has taught me, particularly in murder cases, that the matter is a vexatious problem for the jury. Moreover, it is a cause for grave concern with courts, psychiatrists and district attorneys. I know that some alienists have considerable disaffection for the legal test of criminal responsibility. However, it appears to have been the fundamental test throughout judicial history, and whether a change will ever take place remains for future determination.

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## COMPARATIVE COSTS OF VITAMIN C IN FRESH AND COMMERCIALY CANNED FRUIT AND VEGETABLE JUICES\*

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SCURVY has been known on this continent for at least four centuries, or since the days when the French explorer, Jacques Cartier, and his crew were cured of scurvy by tea made from young pine buds and pine needles by a group of friendly Indians.<sup>1</sup> At that early time and for many subsequent years, little was known concerning the material that was present in plants, growing buds, fruits and vegetables and was effective in the prevention or cure of scurvy. Hence it remained for the modern scientists Waugh and King<sup>2</sup> and Svirebely and Szent-Györgyi<sup>3</sup> to isolate the antiscorbutic vitamin from orange and lemon juices and thus pave the way for the rapid progress of recent years.

Tillmans, Hirsch and Hirsch<sup>4</sup> reported a simple method for the determination of vitamin C, which is based on the reduction of 2,6-dichlorophenolindophenol or 2,6-dichlorobenzeneindophenol in acid solution. Many investigators have used this method for determining the amount of vitamin C in both fresh and canned fruit and vegetable juices. A summary of their results was published by Daniel and Munsell<sup>5</sup> and by Fixsen and Roscoe.<sup>6</sup> These writers have prepared excellent bibliographies of the extensive published reports concerning the effect of variety, maturity, soil, season, storage conditions, canning processes and other factors on the vitamin C content of both fresh and canned vegetable and fruit juices.

Since that time other reports concerning the vitamin C content of citrus fruits and vegetables have appeared in the literature—notably those by Metcalfe, Rehm and Winters,<sup>7</sup> MacLinn and Fellers,<sup>8</sup> the Council on Foods of the American Medical Association,<sup>9</sup> Floyd and Fraps,<sup>10</sup> Bessey,<sup>11</sup> Ingalls,<sup>12</sup> McElroy and Munsell,<sup>13</sup> Beacham and Bonney,<sup>14</sup> French and Abbott,<sup>15</sup> DeWitt and Sure,<sup>16</sup> Fellers,<sup>17</sup> Roberts,<sup>18</sup> Richardson, Davis and Sullivan<sup>19</sup> and Harding, Winston and Fisher.<sup>20</sup> However, in spite of the voluminous data, Olliver<sup>21</sup> and Hawley<sup>22</sup> appear to be the only investigators who have reported the comparative costs of vitamin C from natural sources.

Since the economic status of many patients has

to be considered by the physician when prescribing for dietary deficiencies, and since knowledge of the cost of vitamin C from the natural fruit and vegetable sources should be of considerable interest to many large institutions, it seemed desirable to conduct a study to determine the costs of vitamin C from fresh and commercially canned fruit and vegetable juices purchased on the open market.

### PROCEDURE

The oranges, grapefruit and lemons used in this study were bought on the open market from retail stores in Boston and its vicinity. Five different brands of Florida oranges were selected, but only one brand of the California oranges could be procured. Several unidentified brands of oranges were purchased for comparison with the oranges of known identity. The grapefruit were from Florida and Texas, and the lemons were of California origin.

The vitamin C determinations were made on the juices extracted from individual fruits, with the exception of nine samples of orange juice each of which represented the composite juices of several oranges of a single purchase of a given brand. The juice was expressed with a glass fruit reamer and strained through a light cotton 14-mesh strainer to remove seeds and pulp.

The vitamin C determinations were made by combining 2 cc. of the strained juice with 20 cc. of 8 per cent acetic acid in a 50-cc. Erlenmeyer flask and adding the dye solution|| from a microburette until a drop produced a faint-pink end point that remained for at least thirty seconds.

Since exact knowledge concerning the daily human requirements for vitamin C is lacking, and since Olliver,<sup>21</sup> Hawley<sup>22</sup> and others have tentatively assumed 50 mg. as the normal daily requirement for vitamin C, this figure has been used as the basis of computation in the present study.

### FRESH FRUIT JUICES

The results of analyses of freshly extracted orange, grapefruit and lemon juices are reported

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||The dye solution was prepared by dissolving 0.1 gm. of sodium 2,6-dichlorobenzeneindophenol in hot distilled water, making up to a volume of 200 cc. and standardizing against a solution containing 0.1 gm. vitamin C (Celbione, Merck) in 100 cc. of 8 per cent acetic acid, according to the method of Tripp, Satterfield and Holmes.<sup>23</sup>

in Table 1, which includes data concerning the brand, source, weight and cost of the fruits, the volume of juice obtained, the amount of vitamin C per 100 cc. of juice, the volume of juice necessary

### Oranges

The Florida oranges varied in weight from 112 to 232 gm., and cost from 17 to 33 cents a dozen. They supplied from 53 to 96 cc. of juice and

TABLE 1. *Cost of Vitamin C from Fresh Fruit Juices.*

BRAND	SOURCE	WEIGHT	COST PER DOZ	JUICE EXTRACTED	VITAMIN C CONTENT OF JUICE	JUICE REQUIRED TO GIVE 50 MG VITAMIN C	COST OF DAILY VITAMIN C REQUIREMENT (50 MG.)
		gm	cents	cc	mg /100 cc	cc	cents
<i>Orange Juice</i>							
C	Fla	186	75	96	54	93	2.0
D	Fla	173	17	65	52	96	2.1
A	Fla	201	23	81	54	91	2.2
F	Fla	113	23	63	64	78	2.4
A	Fla	205	23	84	45	111	2.5
B	Fla	182	25	63	58	86	2.8
C	Fla	232	33	92	47	106	3.2
F	Fla	112	23	53	41	122	4.4
Average		175	24	75	52	98	2.7
F	Calif	278	40	96	54	93	3.2
F	Calif	160	30	67	59	85	3.2
F	Calif	157	29	74	51	98	3.2
F	Calif	169	18	50	46	109	3.3
F	Calif	182	35	84	45	111	3.3
F	Calif	159	25	77	39	128	3.5
F	Calif	122	18	55	37	135	3.7
F	Calif	161	25	74	37	135	3.8
F	Calif	147	29	71	42	119	4.0
F	Calif	181	35	94	39	128	4.0
F	Calif	276	50	126	34	147	4.9
F	Calif	107	18	44	32	156	5.3
F	Calif	264	50	104	32	156	6.0
F	Calif	242	40	46	49	102	7.4
Average		180	32	77	43	122	4.2
—	Unknown	134	18	70	44	114	2.4
—	Unknown	117	18	60	40	125	3.1
—	Unknown	111	18	55	40	125	3.4
—	Unknown	183	35	79	52	96	3.5
—	Unknown	170	30	90	38	132	3.7
—	Unknown	160	35	80	46	109	4.0
—	Unknown	170	30	78	27	185	5.9
Average		151	26	73	41	127	3.7
Average of all brands		172	28	75	45	116	3.7
<i>Grapefruit Juice</i>							
J	Fla	519	60	183	39	128	3.5
G	Fla	634	100	230	47	106	3.8
F	Fla	480	100	188	48	104	4.6
I	Fla	528	100	201	43	116	4.8
G	Fla	641	100	210	41	122	4.8
I	Fla	499	100	186	42	119	5.3
G	Fla	423	100	175	43	116	5.5
Average		532	94	196	43	116	4.6
H	Texas	485	100	168	59	85	4.2
H	Texas	470	100	174	56	89	4.3
H	Texas	418	100	133	65	77	4.8
Average		458	100	158	60	84	4.5
Average of all brands		510	96	185	48	106	4.6
<i>Lemon Juice</i>							
F	Calif	143	40	63	49	102	5.4
F	Calif	155	40	62	50	100	5.4
F	Calif	134	40	64	46	109	5.7
F	Calif	131	40	62	46	109	5.9
F	Calif	140	40	66	43	116	5.9
F	Calif	141	40	55	49	102	6.2
F	Calif	120	40	52	52	96	6.2
F	Calif	106	40	46	55	91	6.6
F	Calif	111	40	49	51	95	6.7
F	Calif	111	40	32	33	151	15.7
Average		129	40	55	47	107	7.0

to provide the daily vitamin C requirement of 50 mg. and the cost of this quantity of vitamin C daily. Similar data concerning the canned juices are reported in Table 2.

contained from 41 to 64 mg. of vitamin C per 100 cc. of juice. From 78 to 122 cc. of juice was required to supply 50 mg. of vitamin C at a cost of from 2.0 cents to 4.4 cents. These variations

are in accord with the reports of several investigators. Daniel, Kennedy and Munsell<sup>24</sup> in a study of Florida oranges found 45 to 51 mg. of vitamin C per 100 cc. of juice. Beacham and Bonney<sup>14</sup>

TABLE 2. *Cost of Vitamin C from Canned Fruit Juices.*

BRAND	COST PER CAN	VOLUME OF JUICE PER CAN	VITAMIN C CONTENT OF JUICE	JUICE REQUIRED TO GIVE 50 MG VITAMIN C	COST OF DAILY VITAMIN C REQUIREMENT (50 MG.)
	<i>cents</i>	<i>cc</i>	<i>mg / 100 cc</i>	<i>cc</i>	<i>cents</i>
Tomato Juice					
D	5	414	16	313	3 8
A	10	591	21	238	4 0
H	8	710	14	357	4 0
C	7	414	17	294	5 0
E	9	591	15	333	5 1
L	18	1479	11	454	5 5
F	10	591	15	333	5 6
G	23	1390	14	357	5 9
K	6	384	12	416	6 5
B	10	444	17	294	6 6
I	9	355	14	357	9 1
J	13	532	12	416	10 2
M	10	591	8	625	10 6
Average	11	653	14	368	6 3
Orange Juice					
Y	10	532	44	114	2 1
AA	7	399	37	135	2 4
Z	11	532	41	122	2 5
W	10	355	54	93	2 6
CC	10	532	31	161	3 0
X	10	355	47	106	3 0
BB	9	355	35	143	3 6
Average	10	437	41	125	2 7
Grapefruit Juice					
O	17	1360	37	135	1 7
B	20	1360	34	147	2 2
H	9	532	37	135	2 3
E	9	532	34	147	2 5
Q	9	532	32	156	2 6
R	10	532	32	156	2 9
T	23	1360	27	185	3 1
N	13	532	37	135	3 3
P	13	532	33	152	3 7
V	7	532	18	278	3 7
U	11	532	25	200	4 1
S	15	532	29	172	4 9
Average	13	739	31	167	3 1
Lemon Juice					
X	5	163	45	111	3 4
W	7	170	43	116	4 8
B	9	170	43	116	6 1
EE	10	170	21	238	14 0
DD	10	118	29	172	14 6
Average	8	158	36	151	8 6
Pineapple Juice					
H	10	532	13	385	7 2
GG	25	1360	8	625	11 5
FF	13	532	10	500	12 2
F	13	591	8	625	13 8
GG	7	355	7	714	14 1
B	13	532	8	625	15 3
S	18	532	10	500	16 9
Average	14	633	9	568	13 0
Miscellaneous Fruit Juices					
Papaya					
nectar	17	444	10	500	19 2
Lime	15	116	22	227	28 9
Apricot					
nectar	11	355	2	2500	77 5
Apple	12	591	1	5000	101 5
Cranberry	15	473	1	5600	158 5

state that citrus fruits show considerable variations due to geographic location, varieties and root-stock differences. French and Abbott<sup>15</sup> in a recent study of Florida citrus fruits and vegetables reported that large variations in vitamin C content can be

expected between different varieties of citrus fruits and among samples of one variety. They also found that individual trees produced fruit the vitamin C content of which varied but slightly. Harding, Winston and Fisher<sup>20</sup> in a study of Florida oranges found higher vitamin C values for oranges picked from outside branches of the tree and well exposed to sunlight than for oranges from the interior of the tree.

The Council on Foods of the American Medical Association<sup>25</sup> reported that juice prepared from fresh Florida oranges by reaming and straining through cheesecloth contained an average of 37 mg. of vitamin C per 100 cc. They also found that orange juice maintained in stoppered flasks retained 97.6 per cent of its vitamin C activity after twenty-four hours at refrigerator temperature, and concluded from this evidence that fresh orange juice loses very little vitamin C potency on standing in the refrigerator, especially if protected from air. Ingalls<sup>12</sup> stated:

Oxidation of ascorbic acid in orange, tomato and pineapple juices proceeds so slowly at icebox temperatures that the greater part of their vitamin C potency is retained after one or two days' refrigeration. The longer they stand, however, the greater is the destruction of the vitamin. Although the rate of oxidation is materially increased at room temperatures, and greatly increased by boiling, it is not enough to necessitate particular caution in the ordinary kitchen handling and preparation of these juices.

The California oranges varied from 107 to 278 gm. in weight, and cost from 18 to 50 cents a dozen. They supplied from 44 to 126 cc. of juice, which contained from 32 to 59 mg. of vitamin C per 100 cc. From 85 to 156 cc. of juice was required to supply 50 mg. of vitamin C at a cost of from 3.2 to 7.4 cents. Richardson, Davis and Sullivan<sup>19</sup> reported that California, Valencia and navel oranges supplied from 37.5 to 52.5 cc. of juice and from 20 to 31 mg. of vitamin C per orange. Metcalfe, Rehm and Winters,<sup>7</sup> in a study of six brands of Texas oranges, found the vitamin C content per 100 cc. of juice to vary between 36.6 mg. for navel oranges to 62.3 mg. for a variety known as pineapple oranges. Floyd and Fraps,<sup>10</sup> in an extensive study of the vitamin C content of 217 samples of Texas foods, found that oranges contained from 29 to 46 mg. of vitamin C per 100 gm.

The seven oranges of unknown brand and source varied in weight from 111 to 183 gm., and cost from 18 to 35 cents a dozen. They supplied from 55 to 90 cc. of juice per orange, which contained from 27 to 52 mg. of vitamin C per 100 cc. From 96 to 185 cc. of juice was required to supply 50 mg. of vitamin C at a cost of from 2.4 to 5.9

cents Hawley,<sup>22</sup> Bessey<sup>11</sup> and Ingalls<sup>12</sup> report that fresh orange juice contains about 50 mg of vitamin C per 100 cc, but Daniel and Rutherford<sup>26</sup> found 32 to 62 mg of vitamin C per 100 cc of juice for eight varieties of oranges.

The average values for the Florida oranges were 175 gm in weight, 24 cents a dozen, 75 cc of juice per orange, 52 mg of vitamin C per 100 cc of juice; 98 cc of juice supplied 50 mg of vitamin C at a cost of 27 cents. The values for California oranges were 180 gm in weight, 32 cents per dozen, 77 cc of juice per orange, 43 mg of vitamin C per 100 cc of juice, 122 cc of juice supplied 50 mg of vitamin C at a cost of 42 cents. The averages for the oranges of unknown source were 151 gm in weight, 26 cents per dozen, 73 cc of juice per orange, 41 mg of vitamin C per 100 cc of juice, 127 cc of juice supplied 50 mg of vitamin C at a cost of 37 cents. Oliver,<sup>21</sup> an English investigator, found that 50 mg of vitamin C in orange juice cost 2½ pence, Hawley<sup>22</sup> reports the cost as 35 cents.

### *Grapefruit*

The Florida grapefruit varied from 423 to 641 gm in weight and cost from 60 cents to \$1.00 a dozen. They supplied from 175 to 230 cc of juice, which contained from 39 to 48 mg of vitamin C per 100 cc of juice. From 104 to 128 cc of juice was required to supply 50 mg of vitamin C at a cost of from 35 to 55 cents.

The Texas grapefruit varied from 418 to 455 gm in weight, all cost \$1.00 a dozen, and contained from 133 to 174 cc of juice. The juice contained from 56 to 65 mg of vitamin C per 100 cc of juice. From 77 to 89 cc of juice was required to supply 50 mg of vitamin C at a cost of from 42 to 48 cents. Olliver<sup>23</sup> states that 50 mg of vitamin C in fresh grapefruit juice costs 4½ pence, and Hawley<sup>22</sup> found the cost for this amount of vitamin C to be 35 cents.

The average values for grapefruit were 510 gm in weight, 96 cents per dozen, 185 cc of juice, 48 mg of vitamin C per 100 cc of juice, 106 cc of juice supplied 50 mg of vitamin C at a cost of 46 cents.

### *Lemons*

The lemons, all from California, varied from 106 to 155 gm in weight, cost 40 cents a dozen and supplied from 32 to 66 cc of juice, which contained from 33 to 55 mg of vitamin C per 100 cc of juice. From 91 to 151 cc of juice was required to supply 50 mg of vitamin C at a cost of from 54 to 157 cents. Richardson, Davis and Sullivan<sup>19</sup> found an average of 49 mg of vitamin C per 100 cc in California lemons. Lund, Spur

and Friderici<sup>27</sup> report that the vitamin C content of lemon juice varied from 39 to 56 mg per 100 cc. Olliver<sup>23</sup> found that 50 mg of vitamin C in lemon juice cost 3¼ pence.

The average values for lemons were 129 gm in weight, 40 cents per dozen, 55 cc of juice and 47 mg of vitamin C per lemon; 107 cc of juice supplied 50 mg of vitamin C at a cost of 70 cents.

### *CANNED FRUIT AND VEGETABLE JUICES*

The canned tomato, orange, grapefruit, lemon and pineapple juices and a series of five less important fruit juices were purchased from retail stores in Boston and its vicinity. That the data obtained might be of fairly general application, thirteen brands of tomato juice, seven brands of orange juice, twelve brands of grapefruit juice, five brands of lemon juice and seven brands of pineapple juice were assayed. Since there was a wide range in size of containers and cost for the individual canned fruit juices, no attempt was made to correlate prices with the volume of juice per can. The canned fruit juices were not strained, but the canned tomato juices were centrifuged for ten minutes at 1300 r.p.m. or until a clear yellow supernatant liquid appeared. A 5 cc portion of the supernatant layer was used for assay, instead of the 2 cc portion that was used in the assay of the fresh fruit juices.

#### *Tomato Juice*

The thirteen samples of canned tomato juice varied in vitamin C content from 8 to 21 mg, and averaged 14 mg of vitamin C per 100 cc. The amount of juice necessary to provide 50 mg of vitamin C varied from 238 to 625 cc, with an average of 368 cc. The cost of 50 mg of vitamin C in tomato juice varied from 38 to 106 cents and averaged 63 cents, a figure that is materially higher than the 475 cents reported by Hawley.<sup>22</sup>

Ingalls<sup>12</sup> stated that canned tomato juice contains 17 mg of vitamin C per 100 cc, which is in close agreement with 14 mg of vitamin C per 100 cc found in this study. A series of 132 cans of commercially canned tomato juices tested by McElroy and Munsell<sup>11</sup> averaged 17 mg per 100 cc of juice. McClinn and Fellers<sup>8</sup> have published an excellent bulletin, which reports in great detail the vitamin C content of tomatoes and tomato products as affected by such conditions as canning, storage, maturity, fertilizers and many other factors. They found that commercial brands of tomato juice contained from 7 to 18 mg, with an average of 11 mg of vitamin C per 100 cc of juice. Tressler and Curran<sup>28</sup> found that little or no loss of vitamin C occurred at the end of forty



days' storage of tomato juice in either bottles or cans completely filled with hot juice.

### *Orange Juice*

The vitamin C content of the canned orange juices varied from 31 to 54 mg., and averaged 41 mg. per 100 cc. The juice required to provide 50 mg. of vitamin C varied from 93 to 161 cc., and averaged 125 cc. The cost of 50 mg. of vitamin C in canned orange juice varied from 2.1 to 3.6 cents and averaged 2.7 cents; this figure is only a little over half the cost reported by Hawley,<sup>22</sup> who states that 50 mg. of vitamin C in canned orange juice cost 4.25 cents. Mack, Fellers, MacLinn and Bean<sup>23</sup> found 37.7 mg. of vitamin C per 100 cc. for canned orange juice.

### *Grapefruit Juice*

The vitamin C content of the canned grapefruit juice varied from 18 to 37 mg., with an average of 31 mg. per 100 cc. The juice required to provide 50 mg. varied from 135 to 278 cc., with an average of 167 cc. The cost of 50 mg. of vitamin C varied from 1.7 to 4.9 cents and averaged 3.1 cents, which is in fairly close agreement with 2.8 cents reported by Hawley.<sup>22</sup> Roberts,<sup>18</sup> in a study of the keeping qualities of vitamin C in canned grapefruit juice, found an average loss of 25 per cent at the end of nine to fifteen months. Bessey<sup>11</sup> stated that canned grapefruit and orange juices are about 70 to 90 per cent as potent in vitamin C as the fresh juice, and like most canned products remain stable while unopened but slowly lose their vitamin C when left open to the air. Fellers and Isham<sup>30</sup> reported that commercially canned orange juice, orange slices, grapefruit juice and grapefruit slices after nine months' storage contained fully as much vitamin C as fresh fruits.

### *Lemon Juice*

The vitamin C content of canned lemon juice varied from 21 to 45 mg., and averaged 36 mg. per 100 cc. The volume of juice necessary to provide 50 mg. of vitamin C varied from 111 to 238 cc., with an average of 151 cc. The cost of 50 mg. of vitamin C in canned lemon juice varied from 3.4 to 14.6 cents, and averaged 8.6 cents.

### *Pineapple Juice*

The vitamin C content of seven samples of pineapple juice varied from 7 to 13 mg., with an average of 9 mg. per 100 cc. These figures are in accord with those published by Ingalls,<sup>12</sup> who also found an average of 9 mg. of vitamin C per 100 cc. The volume of juice necessary to provide 50 mg. of vitamin C varied from 385 to 714 cc., with an average of 568 cc. The cost of 50 mg. of vitamin

C in pineapple juice varied from 7.2 to 16.9 cents, and averaged 13.0 cents.

### *Miscellaneous Juices*

Samples of canned papaya nectar, lime juice, apricot nectar, apple juice and cranberry juice were assayed for their vitamin C content. Even though most of these juices are not of commercial interest as sources of vitamin C, it is interesting to note that some of them are almost devoid of vitamin C. Their vitamin C content per 100 cc. of juice varied from 1 mg. for canned apple and cranberry juices to 22 mg. for canned lime juice. The amount of juice required to supply 50 mg. of vitamin C varied from 227 cc. of lime juice to 5000 cc. of apple and cranberry juices. The cost of 50 mg. of vitamin C in these juices varied from 19.2 cents for papaya nectar to 158.5 cents for cranberry juice.

### SUMMARY AND CONCLUSIONS

Since a number of investigators have tentatively assumed that 50 mg. of vitamin C represents the normal daily human requirement, the cost of vitamin C from the fresh and canned fruit and vegetable juices has been estimated on that basis. The average amounts of juices required to supply 50 mg. of vitamin C, arranged in ascending order, are as follows: 106 cc. of fresh grapefruit juice, 107 cc. of fresh lemon juice, 116 cc. of fresh orange juice, 125 cc. of canned orange juice, 151 cc. of canned lemon juice, 167 cc. of canned grapefruit juice, 368 cc. of canned tomato juice and 568 cc. of canned pineapple juice. The average amounts of vitamin C per 100 cc. were found to be 48 mg. for the fresh grapefruit juice, 47 mg. for fresh lemon juice, 45 mg. for fresh orange juice, 41 mg. for canned orange juice, 36 mg. for canned lemon juice, 31 mg. for canned grapefruit juice, 14 mg. for canned tomato juice and 9 mg. for canned pineapple juice.

The average cost of 50 mg. of vitamin C from the various sources under consideration was found to be 2.7 cents for canned orange juice, 3.1 cents for canned grapefruit juice, 3.7 cents for fresh orange juice, 4.6 cents for fresh grapefruit juice, 6.3 cents for canned tomato juice, 7.0 cents for fresh lemon juice, 8.6 cents for canned lemon juice and 13.0 cents for canned pineapple juice.

Since vitamin C is stored in the body for only short periods of time, a constant supply is necessary for the promotion of good health. In this study the average cost per year for a daily supply of 50 mg. of vitamin C from the various sources under consideration has been calculated as \$9.86 for canned orange juice, \$11.32 for canned grapefruit juice, \$13.51 for fresh orange juice, \$16.79 for

fresh grapefruit juice, \$23.00 for canned tomato juice, \$25.55 for fresh lemon juice, \$31.39 for canned lemon juice and \$47.45 for canned pineapple juice.

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## MEDICAL PROGRESS

### PHARMACOLOGY

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BOSTON

IN reviewing the pharmacologic literature for 1940-41, one is struck by the stream of basic research that has continued through the past few years. Some of this has been fruitful; other lines have led to conclusions that will be long delayed in practical application. The most valuable practical developments have, of course, been in the study of the sulfonamide drugs. Although they are not directly concerned in this report, it is pertinent to include certain theoretical observations, which may have clinical bearing. Of great importance in this connection is the inhibitory effect of *p*-aminobenzoic acid on the bacteriocidal action of sulfone compounds. Two phases of this action, which seem indubitably established, are worth emphasis.

First, from a theoretical point of view, it is interesting to call attention to the fact that this

inhibiting substance has been recently identified as a part of the vitamin B complex. Offhand, this suggests that excessive amounts of this vitamin might conceivably interfere with the efficacy of these drugs. In these days of indiscriminate exhibition of vitamin substances, this warning may not be so absurd as it sounds at first hearing.

The second matter of practical interest in relation to this inhibition lies in another chemotherapeutic triumph that is often neglected. It has been shown that local anesthetics of the procaine series contain this grouping and, indeed, that it is necessary for local anesthetic effects to be manifest in members of this series of drugs. The conclusion is inescapable, and the actual observation has been made, although not yet published, that the use of large quantities of local anesthetic agents containing the *p*-aminobenzoic acid grouping is contraindicated under circumstances in which interference with the action of sulfonamide drugs is undesirable. This thought must not be carried too far, since local anes-

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thetics are rapidly excreted, but presumably some degrees of inhibition of sulfonamides could operate for twenty-four hours after the use of such substances, and it is not difficult to think of situations in which even this effect would be undesirable.

Work reported in previous reviews on the action of various sympathomimetic drugs continues, without reaching any very certain conclusions. It is increasingly evident, however, that changes in chemical configuration in substances related to epinephrine may alter certain actions without affecting others or may affect various ones in opposite directions. It is essential, therefore, to realize the possibility of undesirable side actions in new members of this series that may come on the market. An excellent review of this subject so far as it relates to amphetamine is that of Cameron and Kasanin,<sup>1</sup> who rightly point out that many of the so-called "sympathomimetic amines" do not really possess this action in toto but only some parts of it.

The digitalis question is still the main preoccupation of certain pharmacologic laboratories. Investigations have been concerned largely with criteria of potency. These are ultimately designed to predict potency in man. As Gold and his co-workers<sup>2</sup> have well pointed out, Pope's old maxim holds for digitalis: "The proper study of mankind is man." It is evident that various digitalis bodies may be compared only by using the same test objects, and Gold insists that all digitalis should be standardized on man—in one sense this is true, but for practical purposes, it is evident from the modern work that in any *one* substance, relative potencies of different preparations may be determined with sufficient accuracy by the current methods of bioassay.<sup>3</sup> However, if one wishes to compare the potency of Lanatoside C, for example, with ouabain, they must be compared on the same test object,<sup>4</sup> and if they are to be compared on man, man is the proper test object. On the other hand, if one is using various preparations of Lanatoside C in the treatment of heart disease, a guide to the relative potency of various samples is afforded by bioassay on animals. Variations in absorption have also been studied.<sup>5</sup> Reference should also be made to the accurate observations of the Cornell group concerning the effects of digitalis on heart rate and efficiency.<sup>6</sup>

In the field of morphine action, progress is developing. Slaughter, Parsons and Munal's<sup>7</sup> emphasis on the cholinergic actions of morphine has led to fruitful explanations of a number of phenomena observed in morphine addiction and therapeutic use. Although their suggestion that

the use of prostigmine enhances the pain-relieving qualities of morphine has not met with universal confirmation, the experimental background is sufficiently clear to make persistence in developing this idea a worthwhile undertaking. Van Duzen, Slaughter and Winter<sup>8</sup> have recently studied the effects of Trasentin, a new synthetic atropinelike drug, and found it capable of counteracting the cholinergic actions of morphine. This recently introduced chemical has been studied in animals, and although it is different in many respects from atropine in its action and bears some resemblance to the action of papaverine, it appears to be worth further clinical trial—especially to relax bladder spasm.<sup>9</sup>

Caffeine and other diuretics have continued to share in pharmacologic interest. Too little work has been done with these substances by the modern methods of studying kidney function developed by Smith and his associates.<sup>10</sup> Evidence for the extrarenal action of caffeine was believed by Vollmer,<sup>11,12</sup> to be indicated by the fact that, in the rat, the output of chloride and potassium was increased by smaller doses than those required to increase the output of sodium. There is, likewise, some indication of extrarenal factors in the experiments of Swigert and Fitz<sup>13</sup> on the diuresis produced by mersalyl. Studies by Bodo and Bloch<sup>14</sup> on the effect of hypnotics and anesthetics on the diuresis of dogs with diabetes insipidus suggest some interesting possibilities in that striking differences in the diuresis-inhibiting effects of these drugs appeared evident. Some hypnotics failed to produce this inhibition, whereas others exhibited this property to a high degree. Additional work on caffeine is contributed by Barmack.<sup>15</sup> He points out that the boredom inseparable from repeated psychologic testing has a hypnotic quality, and he makes the ingenious suggestion that the apparent favorable effect of caffeine on psychologic performance may be due to its antihypnotic effect. Wolff and his co-workers<sup>16</sup> found caffeine to have no pain-threshold elevating power. The psychologic effect of mixtures of drugs to relieve pain seemed to have some weight in the results obtained by these workers. Unpublished evidence<sup>17</sup> indicates that caffeine counteracts the effect of certain analgesic drugs on peripheral pain thresholds and measurably lowers these thresholds. In this connection, it has been aptly pointed out that various alcoholic beverages are effective in proportion to their alcoholic content.<sup>18</sup> It should not be forgotten that alcohol is an effective analgesic agent.

Wolff and his co-workers<sup>19</sup> have also made measurements on the relative efficiency of morphine and certain related compounds in raising

the thermal pain threshold of the forehead. In general, Dilaudid was ten times as efficient as morphine, and morphine was two or three times as effective as codeine. Twenty milligrams of Pantopon was the equivalent of only 8 mg of morphine in these experiments, although previous experiments suggested that Pantopon is nearly as effective as the morphine it contains (that is, two thirds). Apparently, these workers found some antagonism between these opiates and epinephrine, which is to be expected if Slaughter's contention, that the pain-relieving action of morphine is also cholinergic, is correct.

Experiments on local anesthesia continue in the search for new and better agents, but occasional work dealing with clinical applications appears. The effects of epinephrine added to procaine and cocaine are well known. Small quantities are without effect, whereas concentrations greater than 1:50,000 markedly increase toxicity. Ephedrine in small doses diminishes the toxicity of cocaine, and in larger quantities increases it, but exerts no effect on the toxicity of procaine.<sup>20</sup> In a careful histologic study, Salm<sup>21</sup> showed that quinine salts in 1 per cent solution produce actual degeneration of nerve fibers. Although slight degeneration of a very few fibers was demonstrable after injections of physiologic saline solution into nerve fibers, the effect was in no way comparable with the destruction produced by the same quantity of quinine or quinine and urea hydrochloride. The effects of the saline solution are probably due solely to local pressure. It is evident that such effects argue strongly against the use of quinine and urea hydrochloride as a local anesthetic.

The effect of drugs on the action of hormones and vitamins is certain to be a subject of vital interest as time goes on, as demonstrated by the work of Samuels et al.<sup>22</sup> Salicylates increased strikingly the excretion of ascorbic acid. This increased excretion continued as long as the drugs were given. Caffeine and cinchophen produced a similar but much smaller increase in excretion. Single doses of salicylates produced a sharp rise followed by a compensatory fall. The practical implications are obvious.

Many more interesting "leads" appear to have been uncovered during the year, but at the moment, these are of theoretical rather than of practical interest. As their therapeutic implications develop, they will become appropriate topics in future reviews.

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 27281

#### PRESENTATION OF CASE

A fifty-two-year-old single librarian entered the hospital for study.

The patient stated that she had always been very nervous, but had had no specific complaints until six months before admission, when she developed anorexia and a feeling of abdominal distention sometimes associated with constipation. These symptoms were relieved by exercise, but the period was marked by the appearance of exertional dyspnea and palpitation. Primarily for the latter symptoms, the patient consulted her physician, who prescribed iron, with some benefit. She carried on until nine days before entry, when the above symptoms became exaggerated and feverishness developed. Two days later, she apparently caught cold, with nasal obstruction and cough with small amounts of phlegm, which came from the nasopharynx. Three days before admission, she again consulted her physician because of dyspnea, which had become the most troublesome of her symptoms.

For the preceding two years the patient had noticed hot flashes, with a scanty menstrual flow, occurring about every eight weeks. From time to time during the previous year she had suffered from pruritus of the vulva and anus. All these symptoms had been controlled by osteopathy.

The patient's father had died at sixty-five of heart disease, her mother at sixty of cancer of the bladder. She had suffered from the usual childhood diseases, diphtheria and psoriasis.

On examination, the patient was well developed, well nourished and moderately short of breath. There was slight distention of the neck veins. Examination of the fundi showed thickening and tortuosity of the arteries, with arteriovenous nicking. The heart was enlarged to the right and left, and the sounds were forceful and regular, without murmurs. The aortic second sound was greater than the pulmonic; the blood pressure was 180 systolic, 125 diastolic. There were dullness to percussion and rales at the right lung base. In the abdomen there was a slight suggestion of shifting dullness, but no fluid wave. On pelvic examination, the hymen was found to be intact; by rectum, an irregular, slightly tender mass the

size of a grapefruit was found to be jammed but not impacted in the pelvis. An area anteriorly was unusually tender.

The temperature was 101°F., the pulse 140, and the respirations 24.

The urine showed a + test for albumin. The blood showed a red-cell count of 5,190,000 with a hemoglobin of 15.3 gm. (photoelectric-cell technique), and a white-cell count of 15,000 with 76 per cent polymorphonuclears. The nonprotein nitrogen of the blood serum was 15 mg. per 100 cc., the sedimentation rate 25 mm. in one hour. A blood culture and a Hinton reaction were negative.

An x-ray film of the chest showed the heart shadow to be grossly increased in size. The enlargement affected all chambers, but was most marked in the region of the left ventricle. Fluoroscopically, the pulsations of the heart were extremely weak, but the shape did not suggest pericardial effusion. The aorta was somewhat tortuous, but not dilated. The right costophrenic angle was obliterated by a small quantity of fluid; the lung fields were clear.

An electrocardiogram showed partial heart block, with a PR interval of 0.32 second and an occasional dropped beat. The ventricular rate was 125, and there was low voltage of all complexes in Leads 1, 2 and 3.  $T_1$ ,  $T_2$  and  $T_3$  were low or slightly diphasic;  $T_4$  was rather low.

The patient was given digitalis, and showed considerable subjective and objective improvement for a week or more. Two weeks after admission, an electrocardiogram showed normal rhythm with delayed auriculoventricular conduction, a rate of 95 and a PR interval of 0.25 second. There were low-voltage QRS complexes and low T waves, with an almost flat  $T_1$ ;  $ST_2$  and  $ST_3$  were depressed. The white-cell count was 15,000, the sedimentation rate 33 mm. in one hour. An x-ray film of the chest showed an increase in the amount of fluid in the right pleural cavity since the last observation, the fluid extending along the axillary line and in the interlobar fissure. The heart shadow was grossly increased in size, and the pulsations were barely visible. A few days later, the white-cell count was 18,200. An electrocardiogram showed a rate of 120 and delayed auriculoventricular conduction, with a PR interval of 0.23 to 0.24 second; there were low voltage, low  $T_1$  and slight sagging of  $ST_2$  and  $ST_3$ . On the twenty-second hospital day, the patient got out of bed to be weighed, and experienced sudden palpitation and dyspnea without pain. On examination she was orthopneic and cyanotic; the pulse was 88 and rather irregular. The heart

sounds were of poor quality, and there was fluid at the right lung base, with rales at both bases posteriorly.

Death occurred the following day.

#### DIFFERENTIAL DIAGNOSIS

DR PAUL D. WHITE: "Examination of the fundi showed thickening and tortuosity of the arteries, with arteriovenous nicking." Here are indications of changes of the fundi due to hypertension, and later the story suggests heart involvement that may have been secondary to hypertension. Are there any more blood pressure readings?

DR TRACY B. MALLORY: None are recorded. Dr. Fitzhugh, do you have further information?

DR GREENE FITZHUGH: The patient's blood pressure was normal when I saw her in my office about six months before entry to the hospital. The heart examination was essentially negative, and a rectal examination at that time showed no pelvic mass such as was found at the time of entry to the hospital. The patient came in because of pruritus. She did not return, and was seen by an osteopath until three days before entry.

DR WHITE: There is no statement about the liver. Was it felt?

DR MALLORY: One examiner thought he perhaps felt the liver down two fingerbreadths.

DR WHITE: There was evidently no appreciable liver enlargement.

There is some question whether the mass felt by rectum was responsible for the constipation and the difficulties at the beginning of the history, that is, the abdominal distention, anorexia and constipation. What was this mass—tumor or abscess; if tumor, ovarian or uterine, benign or malignant? It hardly seems likely that it was an abscess, and we shall return to the question of neoplasm later.

Weak cardiac pulsations on fluoroscopic examination are most often due to weak action of a large heart, but they may, of course, be caused by pericardial effusion or constriction.

The question comes up whether the pleural fluid was congestive or exudative, and whether there was anything else there, such as a lung infarct. For the lung hilar shadows, may we see the x-ray films? If the heart is very large, it may hide some of the hilar shadows, a fact about which we should like very much to know.

DR JAMES R. LINGLEY: The heart shadow is moderately increased in size, and there is a small quantity of fluid at the right lung base posteriorly in the costophrenic angle. The lungs are otherwise clear. I fluoroscoped the patient myself and was very much struck by the absence of cardiac

pulsations. It seemed more than one would expect with heart failure alone. Yet the shape of the heart did not suggest effusion. Furthermore, the clinicians at the time told me that the sounds were of good quality. That seemed quite unusual to me. The shape of the heart is not abnormal, but there is generalized enlargement. This later film shows increase in the amount of pleural fluid at the right base.

DR WHITE: Is there anything besides fluid?

DR LINGLEY: That is all I can make out. The fluid is extending into the interlobar septum at this point, but so far as I can see, the lungs are clear.

DR WHITE: There is fair evidence that the patient had hypertensive disease, based on examination of the fundi and on the enlargement of the heart. Certainly there was congestive failure.

The heart block is intriguing but not diagnostic. It hardly seems likely that digitalis was responsible, which leaves the following possibilities in the order named: coronary disease, complicating the hypertensive heart disease but without anginal pain; severe rheumatic myocardial lesions, which can occur in persons as old as this; and, as extreme rarities, neoplastic invasion of the heart, marked toxemia and, as in one or two cases we have encountered here, pulmonary embolism.

The febrile course, at least for a month, may be explained in a variety of ways, but not by congestive heart failure. Pulmonary infection and pulmonary infarction are the two best bets. Either one might explain the increase in dyspnea and death, but I think pulmonary infarction is more likely. It would readily explain the sudden episode the day before the patient died. Moreover, she had fever before she caught cold, according to the early history of the present illness. Rheumatic pancarditis, accounting for the heart block and fever, is another important possibility to be considered seriously, but the absence of antecedent rheumatic infection or heart disease is against it. The possibility, however, of a combination of rheumatic infection and pulmonary infection or infarction must be considered. Necrosis from extensive neoplastic disease, with thoracic metastases, is another but more remote possibility as a cause of the fever.

Finally, the pelvic tumor is of interest and perhaps of importance. I was inclined to pass it over on first reading. On second reading it occurred to me that it might explain everything, serving as a primary source of metastatic malignancy in the chest involving the lungs and pleura and even the pericardium, and the heart to explain

the heart block. I have never seen neoplastic heart block, but such cases are on record, although they are exceedingly rare. Then, on further reflection I decided that the pelvic tumor was very likely a red herring.

There is no statement in the record as to whether the mass was hard; it simply mentions an irregular tender mass the size of a grapefruit.

DR. FITZHUGH: It was moderately hard. The gynecologist thought it was a fibroid that had been overlooked at the previous examination.

DR. WHITE: I do not believe it was necessarily responsible for the final illness, unless the tender spot consisted of thrombosed veins that gave rise to the pulmonary embolism. However, Dr. Meigs,\* in his monograph on pelvic tumors, records one type of ovarian tumor, the Krukenberg tumor, that usually originates in the stomach and metastasizes to the ovaries and other parts of the body—the peritoneum, the lungs and even the heart. That may have happened here, but I cannot make a diagnosis on the data we have.

I should favor, in conclusion, the diagnoses of hypertensive heart disease and of congestive failure, complicated by recurrent pulmonary embolism, which finally caused death, arising quite likely from a pelvic thrombosis that complicated a fibroid tumor of the uterus or an ovarian tumor. I should not be greatly surprised, however, to learn of such a relatively rare condition as a Krukenberg tumor or another ovarian malignant tumor, with pericardial and myocardial metastases, or even of rheumatic pancarditis complicating the hypertensive state.

DR. J. H. MEANS: I was intrigued with a certain combination of evidence. The patient had a heart that was enlarged in all four chambers. By fluoroscopy the pulsations were noteworthy weak, and the electrocardiogram showed low voltage, with T waves in some leads that might interest one in a diagnosis of myxedema. However, she had a tachycardia, which would not be consistent with that unless Dr. Fitzhugh had been treating her with thyroid.

DR. FITZHUGH: No. She did not look myxedematous, and her basal metabolic rate was close to normal.

DR. MEANS: Does the condition suggest any sort of beriberi type of heart?

DR. WHITE: Beriberi might be mentioned as a possible background, although it could not explain the final illness; but I should not consider it seriously.

DR. HOWARD B. SPRAGUE: Do you think she could have had multiple myocardial infarcts?

DR. WHITE: In spite of the total absence of pain? One can have painless myocardial infarction, of course. Do you mean that the final episode might have indicated another myocardial infarct?

DR. SPRAGUE: Possibly.

DR. WHITE: I think that in view of the heart block we should diagnose some coronary disease complicating the hypertension, although we have seen heart block in other conditions, such as rheumatic infection and even pulmonary embolism. I do not believe that the heart block is specific enough to help in the diagnosis of coronary disease. With the absence of pain or of characteristic changes in the electrocardiogram I should not want to diagnose multiple myocardial infarction.

DR. FRANCIS R. DIEUAIDE: Is not the variation in the PR interval against any such possibility as a tumor involving the heart?

DR. WHITE: I do not know. There are so few cases on record that I cannot answer your question.

DR. DIEUAIDE: Unless you interfered with the delay by medication, you would not expect it to come down.

DR. WHITE: There is a great deal of variation in PR intervals in heart disease without much obvious change otherwise. But there may also be a change toward improvement when a heart rate drops, the PR interval decreasing. This may be due to an improved local coronary circulation to the bundle of His and its branches. There are too many factors controlling the PR interval to permit easy interpretation of its changes. The variations here, for example, do not rule out, I believe, metastatic myocardial neoplasm.

#### CLINICAL DIAGNOSES

Arteriosclerotic heart disease.

Pulmonary infarction?

Coronary occlusion?

#### DR. WHITE'S DIAGNOSES

Hypertensive, coronary heart disease, with congestive failure and partial auriculoventricular block.

Pulmonary infarction secondary to phlebitis caused by pelvic tumor.

Ovarian malignant tumor (perhaps the Krukenberg type), with metastases to lungs and pleura, to pericardium (with constriction) and to heart (to produce heart block)?

\*Meigs, J. V. *Tumors of the Female Pelvic Organs*. New York. The Macmillan Company, 1934. P. 213.

Rheumatic pancarditis (with pericardial and myocardial involvement), complicating hypertensive disease?

#### ANATOMICAL DIAGNOSES

Reticulum-cell sarcoma, involving multiple lymph nodes, heart, left ovary and peritoneum.

Pulmonary infarct.

Thrombus of right ventricle.

Fibrinous peritonitis, acute.

#### PATHOLOGICAL DISCUSSION

DR. MALLORY: There was a large ovarian tumor, which was thought on gross examination to be an ovarian carcinoma, and there were numerous implants all over the peritoneum. The retroperitoneal nodes, however, were markedly increased in size, which is rather unusual with ovarian carcinoma. As one progressed upward, it became obvious that the tracheobronchial nodes were also large, and that a large tumor continuous with them had invaded the pericardium. Moreover, a large nodule of tumor was found in the heart itself, which extended a considerable distance into the myocardium, particularly in the region of the interventricular septum. The coronary arteries were not significantly narrowed, and there was no evidence of rheumatic infection, so that I believe we are safe in assuming that the heart block was due to the neoplasm. When microscopic examination was made, it was at once evident that this was not carcinoma but a form of lymphoma, which we classified as reticulum-cell sarcoma.

DR. WHITE: Was it metastatic from the ovary?

DR. MALLORY: To the ovary, I assume. It was presumably primary somewhere in the lymphatic system—where, I could not of course say, since the involvement was so general. There was an infarct of fair size in the lung, which had been present for a considerable period, perhaps a week or two. There was no final pulmonary embolus. The precipitate course of the last twenty-four hours was probably due to a terminal acute peritonitis.

#### CASE 27282

##### PRESENTATION OF CASE

A six-year-old boy entered the hospital complaining of pain in the right flank.

The patient felt perfectly well until four weeks before entry, when he began to have attacks of moderately severe, intermittent, nonradiating pain in the right flank. These attacks lasted about fifteen minutes and at first appeared in the late after-

noon, but thereafter in the early hours of the morning, at which time he would be awakened from a sound sleep. Furthermore, they occurred about twice a night and were accompanied by a desire to urinate. The mother believed that the child was urinating more than usual during the day. There had been no other urinary symptoms, nor change in color of the urine, fever, chills or gastrointestinal symptoms.

The child's birth and development had been normal. He had had measles, chicken pox and whooping cough.

On examination, the patient was well developed and well nourished and in no distress. The heart and lungs were normal; the blood pressure was 90 systolic, 60 diastolic. In the abdomen, there was questionable deep tenderness in the right upper quadrant. The urethral orifice was slightly redened.

The temperature was 99.8°F., the pulse 88, and the respirations 20.

The urine, voided with a normal stream, was cloudy, with a specific gravity of 1.012 and a pH of 5.5. It showed a ++ test for albumin, and the sediment was loaded with white blood cells. Three cultures yielded respectively no growth, *Staphylococcus albus*, and colon bacilli and non-hemolytic streptococci. The blood showed a red-cell count of 3,910,000 with a hemoglobin of 16.5 gm. (photoelectric-cell technic), and a white-cell count of 15,600 with 75 per cent polymorphonuclears. The nonprotein nitrogen of the blood serum was 28 mg., the phosphorus 5.0 mg. and the sugar 77 mg. per 100 cc. A phenolsulfonphthalein test showed 20 per cent excretion of the dye in the first fifteen minutes, and another 10 per cent in half an hour. A repeat test gave 55 per cent excretion in half an hour. The stools were normal. A tuberculin test was negative in a dilution of 1:1000.

An intravenous pyelogram and flat film of the abdomen showed incomplete fusion of the neural arch of the fifth lumbar vertebra, and the left kidney was much larger than the right. The dye was excreted promptly and incompletely demonstrated a normal-sized kidney pelvis on the right and a slightly dilated pelvis on the left. The calyces appeared normal.

Chemotherapy was instituted, and the urine cleared within four days, the white-cell count dropping to 7900; the temperature still spiked to 100°F. each day.

One month after admission, a cystoscopic examination was performed. The bladder appeared normal except for a slightly puckered and retracted right ureteral orifice. Both ureters were



catheterized easily, and a clear, equal flow came from each. One cubic centimeter of phenolsulfonephthalein was given intravenously, and the dye appeared from the left kidney in strong concentration within seven minutes. Ten minutes after injection, slightly dye-tinged urine appeared from the right kidney. A retrograde pyelogram showed a normal kidney pelvis on the left side and a markedly dilated kidney pelvis, with dilated calyces, on the right.

An operation was performed three days later.

#### DIFFERENTIAL DIAGNOSIS

DR. FLETCHER H. COLBY: The history and findings of this case suggest an infection of the urinary tract, and the field becomes narrowed down, I believe, to the right kidney. No intra-abdominal lesion, I think, need be looked for, although we must bear in mind that inflammatory lesions, particularly appendiceal abscesses, may give urinary symptoms, pus in the urine and a very well-developed degree of hydronephrosis from the pressure of the inflammatory mass in the abdomen. Here, however, there is no evidence of localization of symptoms in the abdomen and no evidence of peritoneal irritation, so that I think that any abdominal lesion can be ruled out.

Tuberculosis, I believe, can be eliminated because of the negative tuberculin test. At Lakeville State Sanatorium we have never had a patient with renal tuberculosis who has had a negative tuberculin test. In children, one naturally thinks of some congenital anomaly as a background of trouble. Could this child have had an anomaly of renal blood supply with some obstruction to the ureter, or such a thing as congenital narrowing at the ureterovesicular junction with infection? The absence of the neural arch of the fifth lumbar vertebra is one of the commoner anomalies, and I do not believe it is of any particular significance, but anomalies frequently run in pairs. The lower urinary tract seems to be well ruled out as a cause of trouble from such things as a congenital valve of the posterior urethra, because of the very clear statement that the child voided with a normal stream. So that attention is again focused on the right kidney. A right-sided pyelonephritis certainly seems to be the most obvious diagnosis.

There are two significant features in this protocol. The first are the facts that chemotherapy was instituted, and that within four days the urine became clear but the fever persisted. In other words, this child was not well. We know that collections of pus can rarely be successfully treated by chemotherapy and usually require surgical drainage, so that one cannot help thinking with

this sequence of events — the clearing of the urine and the persistence of the fever — that there was a collection of pus, either inside or outside the kidney. The second significant feature was the absence of any evidence of obstruction to the right kidney when this boy first came to the hospital, and one month later, the obvious development of right-sided renal obstruction.

This intravenous pyelogram was apparently taken soon after the child came into the hospital. Renal function was certainly adequate, but the right kidney did not excrete the dye nearly so well as the left. The left kidney outline looks large, but the right one is not at all well seen, and it would be unfair to compare their outlines on this film. The psoas muscle shows up well on the left, not on the right. The x-ray films taken one month later, at cystoscopic examination, show a fairly well-developed degree of dilatation of the right kidney pelvis and the calyces, whereas the left kidney looks very normal. Its outline is clearly visible. I cannot see the outline of the right kidney. Infection within the kidney itself, such as cortical abscess, would account very well for this picture, with the exception of this development of partial obstruction. Infection in the kidney will cause some degree of dilatation in the pelves and calyces, it is true, but it seems to me that something developed in this one month's stay in the hospital to cause obstruction to the right kidney; the most likely thing appears to be a collection of pus outside the kidney. The most reasonable sequence of events in this case seems to be a cortical infection of the kidney, with the later development of a perinephritic abscess.

DR. WILLIAM B. BREED: The obstruction developed with the decrease in renal function on the left. How do you account for that?

DR. COLBY: I think it was because of the presence of an inflammatory mass outside the kidney causing obstruction.

DR. BREED: Pressing on the ureter on the outside?

DR. COLBY: Yes.

#### CLINICAL DIAGNOSES

Pyelitis.

Hydronephrosis.

#### DR. COLBY'S DIAGNOSES

Chronic pyelonephritis.

Perirenal abscess.

#### ANATOMICAL DIAGNOSES

Double kidney.

Chronic pyelonephritis.

Hydronephrosis.

## PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: Dr. Smith, will you give us your preoperative diagnosis and describe your findings?

DR. GEORGE G. SMITH: Our diagnosis was hydronephrosis. I shall read the operative note.

Through a right oblique kidney incision, the kidney was easily freed and delivered and proved to be a double kidney, the upper half of which was plump and smooth, about 6 cm. in length, and drained by a normal appearing ureter. The lower half was drained by a large hydronephrotic pelvis and thickened and dilated ureter. The cortex was almost entirely destroyed, and the line of demarcation between the two halves of the kidney was very clear. Both ureters were followed down to the brim of the pelvis, at which point they were still separate. The ureter from the lower half was clamped cut and tied. The arteries supplying blood to the lower half, which consisted of a group of small vessels on each aspect of the kidney, were tied and divided. The lower half of the kidney was then separated from the upper half through the avascular line. The area thus made in the lower pole of the upper half was closed by two mattress sutures and a few superficial ones. Gerota's fascia below the kidney was sutured to the erector spinae muscle in two places. A rubber drain was left posterior to the kidney. The wound was closed in layers.

DR. MALLORY: I think it is safe to assume that there must have been a stricture of one of the two ureters on the right side at the point where it passed into the bladder, although the exploration was not carried far enough actually to demonstrate it.

DR. SMITH: On looking over the evidence afterward, I thought we might have made the correct diagnosis preoperatively if we had compared the films more carefully. This intravenous pyelogram

shows the ureter coming up here to a small pelvis close to the spine. The ureteropelvic junction, as I demonstrated it with the retrograde pyelogram, is 5 cm. lower and more lateral. I never compared these two films; if I had, I think I should have noticed the difference in the course of the ureter, as shown by the intravenous pyelogram and by the retrograde method.

DR. MALLORY: In other words, it was not the same ureter that you saw on the two occasions?

DR. SMITH: No.

DR. COLBY: Why did the dilatation increase?

DR. SMITH: I do not know that it did. There was no excretion on intravenous pyelogram from the lower pole of the kidney, and that was the thing that should have given us a diagnosis.

I might add that if I had done a phenolsulfonephthalein test with a catheter up the ureter and if I had obtained urine from the bladder at the time, as I should have done, I should have obtained the phenolsulfonephthalein that was excreted by the sound, upper half of the kidney. That would have been a confirmatory piece of evidence, but I should probably have attributed it to leakage from one ureter or the other.

DR. MALLORY: Do you think it probable that there was only one mouth to this double ureter in the bladder, or a second mouth that you did not observe?

DR. SMITH: It is possible that there were two, but I am rather inclined to think that there was only one, a Y-shaped ureter.

DR. MALLORY: As I have seen them, there has usually been only one mouth.

# The New England Journal of Medicine

Formerly

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## MENTAL-HYGIENE CLINICS

ALTHOUGH there is little statistical evidence that mental disease is increasing throughout the world, except for such mental casualties as may be precipitated by the present war, its ratio in proportion to other disease at least remains constant. This means that mental disorders continue to constitute a most serious public-health problem. The fatalistic or pessimistic attitude is that some persons are destined to become insane because of their particular heredity or constitution and that, when this happens, they have to be cared for indefinitely in mental institutions or until, *Deo volente*, they are well again.

The average physician seems to be much less interested in the treatment of mental disorders than he is in advances in the therapy of other diseases. The reason for this may be that the

average physician believes there is so little to be done specifically for the mentally ill patient. The answer to this point of view might well be, like Shaw's defense of Christianity, What there is to be done has not been tried.

As indicated in an article in the July 3 issue of the *Journal*, the tendency to lock the door after the horse is gone—that is, to appropriate larger and larger sums for the custodial care of the insane, or for treatment after the disease is fully developed—is not in keeping with the obviously sounder concept of prophylaxis, which is today, almost as a matter of course, part of the treatment of physical disease.

Scientific interest in preventive measures in dealing with mental disorders arose as never before at the beginning of the present century. The advent of Freud and, in 1909, the establishment of the National Committee for Mental Hygiene introduced a feeling of hopefulness, which has persisted. At times and in certain quarters there has been too much enthusiasm in regard to prevention and cure, but on the whole, the shaking and disturbing of the static, pessimistic, nothing-to-be-done attitude have been healthful.

The work of the committee resulted in the establishment of more and more child-guidance and mental-hygiene clinics in this country through the years from 1913 to 1931. Since 1931, although some clinics have been closed, others have been opened, and their value seems to be proved by the fact that almost all have more demands on their resources than they can satisfy.

Unquestionably there are some persons who are destined to become psychotic because of a deep-seated structural or personality defect or predisposition. However, unless one is completely fatalistic about human destiny, believing that education and environmental influences play no part whatever in the paths we take, there can be no doubt that nurture, as well as Nature, has something to do with what happens to us. And it is human to believe in the possibility of change.

In treating any disease, it is not possible to know the proportional value of all the factors that may act in effecting improvement or cure. It would not

be reasonable to assume, however, that factors which have been present and used again and again in successful treatment have no bearing on the cure or amelioration. When children who present difficult behavior problems in unwholesome home environments become tractable and co-operative in more healthful foster homes, it seems fair to assume that the change in environment had some relation to the alteration in behavior.

Ross\* presents statistics that weigh in favor of the value of psychotherapy. Whether or not patients with emotional or mental difficulties are completely cured for all time is comparatively unimportant. No person can be guaranteed against all forms of disease throughout his life span, but countless patients attest to the help they have received from psychotherapy in leading more contented and useful lives. The public and the psychiatrists and mental hygienists themselves would have to be dupes, indeed, to continue the support of psychiatric and mental hygiene clinics for more than a quarter of a century in the absence of fruitful results. Allowing for the gullibility of those who suffer and need help and for the human frailty that permits any system to continue so long as it provides financial gain for its advocates, the evidence is that psychotherapy works, on its own merits.

The clinics cannot be maintained and become increasingly effective through the sole interest of those primarily concerned professionally. Physicians in general, and through them, the public, in families, schools and courts, must recognize the preventive and therapeutic aid that is available and that, through their understanding and efforts, can be increased.

\*Ross T. A. *An Enquiry into Prognosis in the Neuroses* 194 pp. Cambridge, England: Cambridge University Press, 1936.

## DRUG SAMPLES

UNDER "Current Comment" in the January 25 issue of the *Journal of the American Medical Association* appeared an item entitled "Sample Racketeers." This called attention to an abuse which seems so petty as hardly to merit editorial

comment. Subsequent information, however, leads one to believe that it is more widespread than would be thought. Indeed, New York City has added to its sanitary code a regulation specifically forbidding the marketing of packages conspicuously labeled as samples. Little or no evidence of this practice in Massachusetts is apparent. However, if such an abuse can be shown to exist, it is proper for the medical profession to support such legislation if it is presented to the General Court.

Lately, requests have been made that these samples be collected by physicians and be included in shipments for British relief. This movement should be distinctly discouraged, since almost all pharmaceutical manufacturers have donated generous supplies of needed products, and since the scheme would result in a collection of heterogeneous material—some of it of little or no value—that should not be used indiscriminately.

Another facet of this situation suggests a question of the desirability of using the widespread distribution of pharmaceutical samples as a method of advertising. Although, of course, this is primarily a commercial problem, it is apparent that under the new federal Food, Drug and Cosmetic Act there seems to be little logical reason for manufacturing pharmacists to distribute samples through the mail urging the recipient to "try this." The new act makes it mandatory that any preparation shall have thorough clinical trial prior to being put on the market. If such a preparation has complied with the spirit of this act, it should be unnecessary for the individual physician to be annoyed with an accumulation of samples, most of which find their way into the wastebasket or remain as "dust catchers" to the annoyance of the wife, secretary or charwoman who dusts the office.

Elimination of this method of advertising would save time, money, postage and labor, and the price of the finished product to the patient could thus be reduced. Instead of the indiscriminate distribution of samples, free distribution of medicines might be limited to the fulfillment of bona fide requests for substances to be used in investigative work.

## MEDICAL EPONYM

### HUNTINGTON'S CHOREA

George Huntington (1850-1916), of Pomeroy, Ohio, read an essay before the Meigs and Mason Academy of Medicine, Middleport, Ohio, on February 15, 1872, "On Chorea," which was published in the *Medical and Surgical Reporter* (26: 317-321, 1872).

And now I wish to draw your attention more particularly to a form of the disease which exists, so far as I know, almost exclusively on the east end of Long Island. . . . Chorea, as it is commonly known, . . . is of exceedingly rare occurrence there.

The hereditary chorea, as I shall call it, is confined to certain and fortunately a few families. . . . It is attended generally by all the symptoms of common chorea, only in an aggravated degree hardly ever manifesting itself until adult or middle life; and then coming on gradually but surely, increasing by degrees, and often occupying years in its development, until the hapless sufferer is but a quivering wreck of his former self.

R. W. B.

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

RAYMOND S. TITUS, M.D., *Secretary*  
330 Dartmouth Street  
Boston

### DEATH ASSOCIATED WITH SHOCK FOLLOWING A LOW-FORCEPS DELIVERY

A thirty-seven-year-old para II had received adequate prenatal care, having been seen routinely after the third month. Physical examination was entirely negative. The blood pressure was normal—124 systolic, 70 diastolic. The urine contained no albumin; there was no bleeding or other complication during pregnancy.

The patient entered the hospital in labor at term. After a normal labor of twelve hours and after the vertex had presented at the introitus for forty-five minutes, a low-forceps operation was performed. The baby was large, although the specific weight was not given. There was so much difficulty in delivering the shoulders that, even in the absence of hemorrhage, the cervix was inspected; no tear was noted. There was no unusual amount of bleeding. In spite of this, a rapid pulse, low blood pressure and clammy skin immediately developed, and the patient went into shock, from which she died ten hours later.

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

*Comment.* In the absence of post-partum hemorrhage, this death was attributed to shock. Whenever there is extreme difficulty in the birth of the shoulders, rupture of the uterus must be thought of. It is possible that, in spite of a cervix that did not appear to be torn, a tear in the lower segment of the uterus might have existed.

This patient was not transfused. This was an obvious oversight, because transfusion is of inestimable value in shock.

There was no autopsy, and if the report is an honest and intelligent one, shock must have been the cause of death, although rupture of the uterus cannot be ruled out.

## COMMITTEE ON STATE AND NATIONAL LEGISLATION

H. 115, which provided that physicians should register with their town clerks, was passed by the Committee on Ways and Means, with the recommendation "ought to pass." It was, however, referred to the next General Court by the House on June 26.

H. 114, the annual-registration bill, was reported favorably by the Committee on Public Health but was referred to the next General Court by the Committee on Ways and Means; this action was approved by the House on July 3.

Both these bills were opposed by the Society.

HENRY C. MARBLE, *Chairman*

## DEATHS

HOPKINS—FREDERICK E. HOPKINS, of Springfield, died July 1. He was in his eighty-fourth year.

Born in Richford, Vermont, he attended St. Johnsbury Academy and the University of Vermont, receiving his degree from New York University Medical College in 1884. He was formerly consulting laryngological surgeon at the Memorial Hospital, Brattleboro, Vermont, and was a former president of the New England Laryngological and Otological Society.

Dr. Hopkins was a fellow of the Massachusetts Medical Society and the American Medical Association, and held memberships in the American Laryngological, Rhinological and Otological Society and the American College of Surgeons.

His widow, a son, Dr. Frederick S. Hopkins, and six grandchildren survive him.

RYAN—DENNIS M. RYAN, M.D., of Ware, died June 14. He was in his eighty-second year.

He received his degree from the University of Vermont College of Medicine in 1884, and had practiced medicine in Ware for fifty-three years. He was formerly on the staff of the Mary Lane Hospital, Ware. Dr. Ryan was a member of the Massachusetts Medical Society, the American Medical Association and the Brookfield Medical Club.

His widow, three sons and ten grandchildren survive him.

## CARE OF THE SKIN \*

The care of the skin is a prime requisite of health. From infancy to old age it is subjected to various insults from our so-called civilized manner of living.

The infant's tender skin requires the utmost care. For its daily bath only a mild soap should be used, the skin thoroughly dried, and a bland oil applied, followed by dusting a borated talc on the folds of the skin. Final rinsing of diapers with boric acid solution offsets the alkalinity of the urine, and prevents diaper rash. Overheating of the nursery, overclothing and irregular or excessive feeding make infants fretful and irritate their skins. When a rash appears, a physician should be consulted immediately, for impetigo or eczema may be promptly relieved if treated at the onset.

At the school age, the communicable diseases appear. Daily examination of a child's scalp and skin will reveal any contagious disease, daily bath and change of clothing may prevent them. At adolescence, acne with its blackheads, oiliness and pimples makes its appearance and needs treatment. The concept that youth will outgrow this condition may result in its persistence, with resulting scarring and an inferiority complex that may last throughout adult life. The boy or girl at the high school age desires a clear skin, and treatment should begin as soon as the acne appears. Outdoor exercise, careful diet, regular hours and elimination, with suitable local medication will produce excellent results. Creams and massage should be avoided; the former increase the greasiness and the latter spreads the infection. Soap and water cannot be used too frequently at this age, except in those adolescents with dry or eczematous skins.

Adults should become skin-conscious at home, at work and at play. The skin offers protection against the onslaughts of the outside world, if abused it rebels with outbursts that may vary from a simple inflammation of the skin, or dermatitis, to cancer. Fatigue, emotional stress, overeating, overindulgence in alcoholic beverages and constipation register their effects on the skin. Most curable diseases can be prevented. An intact, soft, pliable skin protects against external irritants and micro-organisms, but dryness and the slightest break in its continuity may lead to eczema or infection. Injuries, irritants and unsuitable clothing should be avoided. The last should be lightweight, soft and seasonal. Washable garments should be worn next the skin, and new ones should always be washed to remove the sizing or backfill before wearing, for this sizing may damage the skin.

Concentrated soap mixtures should be thoroughly rinsed from clothing before drying. Too-powerful alkalis are harmful and are too frequently used by laundries. Care should be exercised in the choice of soap or soap powders. Medicated soaps are of no value and should be avoided, especially those containing mercury or resorcin. All dermatologists realize that soap and water are invaluable in the care of the skin, but the excessive use of soap and soap powders causes nearly 20 per cent of all the eruptions that appear on the hands. These are not trivial ones, but may last for months or years, are disabling, and often lead to serious infections. The best soaps contain very little free alkali, superfatted soaps such as shaving soaps are to be preferred. Careful drying of the skin is important. When prolonged or frequent exposure to soap and water is necessary, rubber gloves over cotton gloves should be worn and a soothing cream rubbed into the skin at the end of the day's work. Well

advised lotions often contain glycerin, which is drying and not so beneficial as vaseline, lanolin, or cold cream, used either singly or combined.

The majority of cosmetics are harmless, a few are beneficial. A soothing cream and a bland powder will protect the skin from the dry overheated air of rooms, and from the ravages of the wind, dust and sun. They must be removed with soap and water at the end of the day. In middle age, creams are useful and may prevent dryness and senile changes. Most claims are absurd—wrinkles cannot be eliminated, nor can the skin be nourished; these must be corrected from the inside, not the outside. Creams containing mercury, such as bleaches, should be avoided. The literature on all cosmetics should be carefully read for if cosmetics contain dangerous ingredients it will be noted on the labels or directions. Face powder should not contain orris root or heavy metals. Perfumes should never be applied to the skin before exposure to the sun, for this may lead to a disfiguring permanent discoloration. Hair dyes and rinses, which are really dyes, are dangerous and eventually cause distressing symptoms. Depilatories may be harmful, and deodorants should be used with care. Frequent permanent waving injures the hair, singeing of the hair is a senseless procedure. Lipstick and nail polishes contain sensitizers and may produce eruptions at areas other than the site of application—for example, about the eyes or on the neck.

Speaking of sensitizers recalls the word allergy, which means an altered reactivity, for example, a person reacts unfavorably to a substance that will not affect most people. I believe that everyone has his own pet allergy and that about 10 per cent have allergies or hyper-sensitivities that need medical attention. The substances that cause allergy are called allergens. They are innumerable and result in all types of eruptions—simple swelling of the skin, hives, sores in the mouth, discolorations, painful growths like pimples or boils, dermatitis, eczema and even death. Bromides and sleeping pills are the worst offenders. If a rash occurs while you are taking a medicine, even aspirin, stop taking it, for drugs are common allergens. If you apply an antiseptic to a cut and it becomes red, blistered and itchy, do not use it again, you are probably hypersensitive to it and should consult your physician and tell him what you applied. Allergy can be due to food, pollens, flowers, fungi, cosmetics, clothing, adhesive tape, industrial contacts and physical agents such as heat, cold and sunlight. A sensitivity may develop after years of contact. A woman may use a face powder or cream for years before it causes a dermatitis. People sensitized to nickel may react to the handling of any nickel-plated object, even safety pins. Everyone should learn to recognize the neighboring poisonous plants, especially poison ivy or oak and primrose. The latter should never be allowed in a house.

Painful feet are disabling, and proper care can prevent them. Careful selection of footwear and daily bathing with hot water and baking soda, followed by massage with linolin, will prevent the formation of painful calluses and plantar warts. Careful drying between toes and a borated dusting powder are good preventives of athlete's foot. Its causative factor is a mold or fungus, which is found lurking everywhere for the unsuspecting barefoot. Footwear should be worn at all times, on the beaches or in showers.

Any change in the skin demands prompt expert medical advice. An enlargement of an old mole or blemish or the persistence of a new one should suggest cancer and prompt attention. No one need die of cancer of the skin, it can be cured by early treatment.

\*A Green Lights to Health broadcast given through State WAAAB by Dr. John G. Downing on March 26, 1941 and sponsored by the Public Health Commission of the Massachusetts Medical Society and the Massachusetts Department of Public Health.

## MISCELLANY

### NOTES

The Howe Research Medal, awarded by the Section of Ophthalmology of the American Medical Association, was given this year, for the first time since 1938, to Dr. Walter B. Lancaster, professor of ophthalmology and chief-of-staff, Clinical Division, Dartmouth Eye Institute. This medal is presented "to any person in any country whose researches in ophthalmology or any of the allied branches of surgery have proved to be of distinguished merit." Dr. Lancaster, formerly of Boston, assumed his new duties at Hanover last fall.

At the annual meeting of the American Neurological Association, Dr. Abraham Myerson, professor of neurology (emeritus), Tufts College Medical School, and clinical professor of psychiatry, Harvard Medical School, was elected second vice-president.

## CORRESPONDENCE

### "THE CLOSED-STAFF HOSPITAL"

*To the Editor:* I wish to protest as absolutely false the following statement in an editorial, "The Closed-Staff Hospital," in the June 5 issue of the *Journal*.

In particular they fail to recognize that any member of the medical profession, regardless of the school from which he graduated or the societies to which he belongs, who can demonstrate to fellow members in his community, and to the trustees of the hospital that serves his community, that he is technically equipped, adequately trained, ethical and desirous of keeping constantly up to date in his profession will have no difficulty in obtaining permission to practice in his local hospital, even though it is inspected and certified as meeting the minimum requirements of the American College of Surgeons.

It is general knowledge among physicians that there is definite and complete discrimination on the basis of school alone. For example, in 1937 one of the local hospitals voted to admit to practice in the hospital only graduates of accredited medical schools. How much of this comes from the headquarters at Chicago and how much is of local origin, I do not know. I feel that any discrimination in a competitive profession that gives a monopoly of hospital practice to certain individuals at the expense of other individuals in the same profession and often in the same society, is open to question. The White Cross seeking a monopoly in house and office as well as hospital practice is simply an extension of the same idea.

If membership on a hospital staff were decided by an impartial examination, there could be no feeling of discrimination as there is at present.

MILMAN PEASE, M.D.

Brookfield, Massachusetts

*To the Editor:* I have just read the editorial on closed hospital staffs in the June 5 issue of the *Journal*, and consider it well composed, but unfair in that it fails to mention the evils which rise from hospital oligarchy. Political and personal, rather than professional and ethical, qualifications inevitably influence the selection of staff men, and there arises an intolerable tyranny even over the selected physicians. Their willingness to "clean house" puts them at the mercy of laymen and physicians

more interested in profit or in power than in the practice of good medicine. The threat of exclusion has been used to coerce young doctors into performing suicidal "charity" services, or into guaranteeing the payment of their patients' hospital bills. Capable anesthetists and other specialists have been discouraged by encountering exclusiveness more shameful than that of the "closed shop."

Where county societies exist, active and representative judicial councils correct abuses of medical ethics. A hospital staff is far less likely to give impartial consideration to a physician's ethical and technical qualifications than is such a judicial council, responsible to the entire profession. What council can compel hospital trustees to manumit their medical slaves?

If general practice is to survive, and if medicine is to remain the progressive and personal profession of which we are proud, hospital facilities must remain at the disposal of the entire medical public, and neither religion nor influence nor servility may be the requisites for access to their use.

AUSTIN BLOCH, M.D.

1301 Hepburn Avenue  
Louisville, Kentucky

\* \* \*

In the editorial referred to in the above letters, eligibility was considered a matter to be decided, on the basis of proper professional qualifications, by the hospital rather than by any set rules laid down by another organization. Religion, influence or servility should not enter into the decision; but, if the qualifications stated in the sentence quoted in the first letter are met, the *Journal* is of the opinion that the graduate of a nonapproved medical school would, or at least ought to, have little — possibly "no" — difficulty in obtaining permission to practice in his local hospital. — Ed.

## ELECTROENCEPHALOGRAPHIC STUDIES OF TWINS

*To the Editor:* Under a grant from the Committee on Human Heredity of the National Research Council, we are making a study of the heredity of cortical dysrhythmia. We should appreciate the opportunity to make electroencephalographic records of identical twins of any age, normal or sick, although we should be especially glad to have subjects in whom one or both have a disorder of the central nervous system. The examination causes no discomfort, and the subjects used will be recompensed for time and travel. All who are interested should write or telephone me at the Neurological Unit, Boston City Hospital (KENmore 8600, Extension 654).

WILLIAM G. LENNOX, M.D.

Boston City Hospital  
Boston

## REPORT OF MEETING

### NEW ENGLAND ROENTGEN RAY SOCIETY

A regular meeting of the New England Roentgen Ray Society was held at the Boston Medical Library on April 18, with Dr. George W. Holmes presiding.

The first discussion was by Dr. Claude E. Welch, of the Massachusetts General Hospital, on "Gastric Ulcer and Its Relation to Carcinoma of the Stomach." Gastric ulcer was said to be rare, compared with duodenal ulcer and gastric carcinoma. A study was carried out to confirm a preconceived idea that the clinical and roentgenologic manifestations of gastric ulcer and cancer are similar in a high percentage of cases, that carcinoma resembling

ulcer is a favorable lesion, and that ulcers, therefore, should be treated surgically, especially by subtotal gastric resection. Two hundred and fifty-five cases were studied in which the mortality on medical treatment was 4 per cent, and on surgical management 10 per cent, with a combined figure of 7 per cent. In 39 cases in which the preoperative diagnosis was ulcer, the final diagnosis was cancer, and 17 cases originally classified as cancer were ultimately proved to be benign ulcer. Among the 69 resected cases in which the preoperative diagnosis was obtained from the surgeon, internist, roentgenologist and pathologist, there was a 43 per cent error, by one or more observers, in naming carcinoma benign ulcer. All four were wrong in 26 per cent of the cases. A more serious mistake was the finding of cancer in 17 per cent of posterior gastroenterostomy cases, and in 7 per cent of the medically treated cases, with the latter, 12 of the 13 cases finally reached surgical intervention only after having been followed for more than ten months.

It has been suggested that various criteria may aid in the differentiation of benign and malignant gastric lesions, but these have been evaluated and found wanting in many cases. The age of the patient is probably significant in that there is a high incidence of cancer in the group over fifty years, especially when signs and symptoms have been present for less than one year. Duration is of some value, for the possibility that cancer may cause symptoms for more than five years is unlikely. The site of the lesion is important, for those on the greater curvature are almost 100 per cent malignant and those in the prepyloric region 65 per cent cancerous, whereas ulcers of the anterior and posterior surfaces and of the pylorus are malignant in only 20 per cent and 10 per cent of cases respectively. In regard to the size, it is a fair statement that the percentage of carcinoma is high in large lesions, especially in those more than 2.5 cm in diameter. The amount of hydrochloric acid is significant only if there is none, for carcinoma associated with ulceration has essentially the same amount of acid as a benign ulcer. The rate of healing and the type of pain have been found particularly unreliable as criteria of differentiation.

Of all resected cancers of the stomach, the mortality was 25 per cent, and the five year curability 20 per cent. Of those originally diagnosed as benign ulcer, on the other hand, the mortality was only 10 per cent and the curability 40 per cent. The improved prognosis in the latter group is therefore apparent. The total mortality for all subtotal resections was 9 per cent, and for those previously unoperated on only 6 per cent, as compared with a mortality of 14 per cent in posterior gastroenterostomies. Furthermore the statistics for subtotal resection have been improving with experience, and this operation is strongly recommended because of its low mortality and certain diagnosis. Even in comparison with medical treatment, subtotal resection makes a creditable showing for adding the deaths from cancer (8 per cent) to the operative mortality (6 per cent) gives a total of 14 per cent whereas the medical deaths of 4 per cent when added to the deaths from cancer (13 per cent) amount to 17 per cent.

In conclusion, immediate surgery was advocated in lesions of short duration, especially when the patient is over fifty years of age when the lesion is more than 2.5 cm in size, if there is anacidity, if the site is on the greater curvature or in the prepyloric region, and if there is a chronic lesion on the lesser curvature. Medical management should be tried in acute ulcers, in young patients when the lesion is small, and when the site is in a low cancer incidence area. Such a lesion should heal in one

month and should be checked roentgenographically in another month.

The next presentation was an associated discussion, entitled "The Roentgenologic Similarity of Benign and Malignant Lesions," by Dr James R. Lingley, of the Massachusetts General Hospital. Mobility, size, tenderness, spasm, the presence or absence of rugae, and the location and type of ulcer may give clues when correlated, but no single criterion can ever be routinely relied on for differentiation. Improvement under a medical regimen is no certain indication of the benign character of the lesion, for an ulcerated malignant lesion will often give the same response. Numerous case reports were cited as evidence of the unreliability of any one or even several combinations of these various diagnostic points.

Dr Tracy B. Mallory, of the Massachusetts General Hospital, then discussed "Malignant Ulcers of the Stomach." The differentiation of malignant and benign gastric lesions is often impossible grossly, and exceedingly difficult even microscopically. Carcinoma in situ existing as long as seven years has been proved in the uterine cervix. This noninvasive stage of cancer differs from so-called precancerous lesions in its irreversible character, for the latter may often not progress to malignancy. Carcinoma in situ is autonomous only in its own habitat. Many such lesions have recently been demonstrated in prepyloric ulcers resected at the Massachusetts General Hospital. Photomicrographs demonstrated the differences between normal gastric mucosa, the intestinal metaplasia sometimes seen in normal adults, benign peptic ulcer, with its red fibrinoid layers at the site of active digestion, and ulcerated carcinoma, with its poor regimentation of nuclei and large and irregular mitoses. It was reiterated that ulcerated carcinoma of the stomach has all the characteristics of a benign ulcer. Cancer in situ cannot be determined grossly at operation much less roentgenographically or clinically, and there have been no recurrences in such cases subjected to subtotal resection at the Massachusetts General Hospital. Therefore, this should be the treatment of choice.

Dr Richard Schatzki, of the Massachusetts General Hospital, discussed "The Followup of Patients with Carcinoma of the Larynx." A study of such cases treated by roentgen rays at the Massachusetts General Hospital from 1934 to 1938, usually after being refused surgically, revealed that 11 of 33 patients were alive from three to seven years after treatment. Disappearance of the lesion usually occurs almost immediately, if at all, and recurrence after a year and a half is virtually unknown. The grade of malignancy seems inconsequential as a determinant of curability. Lateral films, as well as bronchoscopy, are employed to locate the site and extent of the lesion. Treatment should consist of large doses over a short period, with no repetition later. Doses of 3000 to 3600 r to each side of the neck, or 300 r per day, are delivered with occasional additional amounts if the immediate result is good and the skin reaction not too marked. Tracheotomy diminishes the chances of cure, and better treatment obviates the need for such a procedure.

Dr LeRoy A. Schall pointed out that cures as high as 80 per cent are obtained by surgical methods in lesions confined to the vocal cords, with a mortality of only 1 per cent and a short hospital stay. Subglottic cancers are not radiosensitive and should be treated surgically if Grade I and probably if Grade II, since a curability rate of 75 per cent is obtainable with laryngofissure. In the more extensive lesions in which laryngectomy was performed 74 per cent of patients are alive without disease. In conclusion it was advocated that the roentgenologist be



given an opportunity to improve these statistics by treating favorable cases.

The roentgenologic treatment of polycythemia vera was discussed by Dr. Laurence L. Robbins, of the Massachusetts General Hospital. Diagnosis is made by the finding of a persistently high erythrocyte count, splenomegaly, a normal oxygen saturation of the blood (in contrast to compensatory polycythémias) and marrow biopsy, if necessary to rule out leukemia. Sixteen patients with thrombophlebitis and bleeding were studied, and remissions up to five years were obtained in 13 cases. A series totaling 500 r is given at the rate of 50 r per day, alternating anterior and posterior portals and using a spray method. Treatment is stopped if the leukocyte count drops below 4000, but all the good responses occurred in cases in which this count was less than 6000. Improvement should appear in less than three months, and another course may be attempted cautiously if there is no response within that period.

The final paper was a discussion, "The Removal of Lipiodol from the Spinal Canal," by Dr. Aubrey O. Hampton, of the Massachusetts General Hospital. Surgical removal at operation has not been successful, whereas the proper suction technic has given good results in almost all cases. The patient is placed face down, with a pillow under the abdomen. An unbreakable needle is inserted between the third and fourth lumbar vertebral spines, since most ruptured intervertebral disks occur in the next space below and should be avoided. Removal is favored by an early carrying out of the procedure, which is now performed as soon as the spinogram has been taken and observed. The entire method requires only thirty to sixty minutes. Suction should be very gentle. Pain indicates improper position of the needle.

## BOOK REVIEWS

*Population: A problem for democracy.* By Gunnar Myrdal. 12°, cloth, 237 pp. Cambridge: Harvard University Press, 1940. \$2.00.

The medical profession helped to create the problem of population pressure, for scientific medicine and the public-health movement have saved lives. It therefore behooves the physician to interest himself in modern aspects of demographic problems.

Although population presses on food in China, India and some other parts of the world, in the United States and in western Europe, until the recent war at least, food pressed on population. Malthus was not wrong. He merely needs to be restated. Professor Myrdal, a distinguished Swedish economist, attempts to do this.

With a net reproduction index of around 0.75, the Swedish population is not reproducing itself. The same condition exists in many American cities. Probably the population of the United States, as a whole, is just about reproducing itself when allowance is made for the excess of women in the childbearing period. Soon we shall have a stationary population.

Will the fears engendered by that condition create many crackpot schemes for increasing population? Professor Myrdal thinks so. He wants Americans to be forewarned, to take thought now, to plan intelligently for the future. He analyzes Swedish conditions in the hope that American scholars may be able to give intelligent guidance in the future. He combines the clear thinking of the scientist and the statistician with a statesman's regard for the long-run welfare of the family and the state.

The author insists that the difficult problem of inducing the healthy and intelligent to reproduce in sufficient numbers must be met within the framework of democratic institutions and not by means of fascist, short-cut methods, intolerable to a free people. Even if more reproduction is needed, it must not be at the expense of the poor, ignorant and unhealthy.

There is no space to analyze in detail Professor Myrdal's economic and social program. Suffice it to say that it recommends, among other things, subsidies in kind (not money) for better housing and nutrition of children without a means test. Married women should be protected in their jobs when they try to combine maternity with a limited career. A more thorough child-welfare program is called for to reduce the burden of those who bear the brunt of the cost of childbearing. The Swedish program should be seriously studied to determine how far it can be adapted to this country before a stationary population is reached in about 1960.

*Compendium Physicac.* By Charles Morton. Compiled about 1680. Publications of The Colonial Society of Massachusetts. Collections: Vol. 33. 8°, cloth, 237 pp. Boston: The Colonial Society of Massachusetts, 1940. \$5.00.

Morton's *Compendium*, here printed for the first time, was circulated among Harvard College students in manuscript from 1687 to 1728 as the textbook in science. Morton wrote it in England about 1680 and brought it to this country in 1686. The book had an immediate effect, as noted in the Commencement theses of 1687. The manuscript has been carefully edited from a number of copies, and a preface on Morton's life has been supplied by Professor Samuel E. Morison of Harvard University. The publication of this volume is an important contribution to the history of science in America by the Colonial Society of Massachusetts. The book has been printed by the Merrymount Press in an impeccable format.

*Bellevue.* By Lorraine Maynard. In collaboration with Laurence Miscall, M.D. 8°, cloth, 280 pp. New York: Julian Messner, Incorporated, 1940. \$2.50.

A great metropolitan hospital is viewed, in newspaper slang, "through the eyes of a woman," with a collaborating doctor. This fast moving book, written for the public, gives what is described as a look "behind the scenes into the human drama of the world's most famous hospital." There is not much of medical interest in the book, and the public must wonder if this is really all that goes on as a routine in a big hospital. Some of the stories are good, but the whole style of the book is theatrical and Hollywoodish.

*A History of Medicine.* By Arturo Castiglioni, M.D. Translated from the Italian and edited by E. B. Krumbhaar, M.D., Ph.D. 8°, cloth, 1013 pp., with 443 illustrations. New York: Alfred A. Knopf, 1941. \$8.50.

This large, well-illustrated history of medicine, by the foremost Italian medical historian, has long been known to scholars in Italian and French editions. An English edition for American and British students, translated from the Italian by Dr. Krumbhaar, a distinguished American scholar, is now at hand.

The book covers the whole field of medicine and is particularly rich, as might be expected, in the glorious history of the Italian contributions to the subject. Much of American history, however, has been skillfully woven

into the text by the translator, and the book remains as a standard, complete text of great value. Not so factual as Garrison's *Introduction*, nor so widely documented as multivolume German surveys of the past, Castiglioni's book nevertheless finds a place in the literature of our time and will be extensively used, without replacing other books. For the average student or physician it can be soundly recommended. This book and Garrison's final edition will long be two cornerstones of a medical history library. Finely printed and illustrated, the book is a credit to American publishing.

*The 1940 Year Book of Pathology and Immunology*  
 Edited by Howard T. Kirsner, MD (pathology) and  
 Sanford B. Hooker, MD (immunology) 12°, cloth, 698  
 pp, with 113 illustrations Chicago: The Year Book  
 Publishers, Incorporated, 1940 \$3.00

This book should prove a welcome addition to the library of the pathologist and bacteriologist. Arranged in the now familiar "year book" form, it is divided into two sections: one on pathology and the other on immunology. The abstracts of important papers are well written and informative. On the whole the difficult problem of choosing papers for review has been well solved. The reprinting of over one hundred illustrations from the original papers adds definitely to the value of the volume. The authoritative scope of this year book would perhaps be enhanced by the inclusion in both sections of the book of more short reviews of the general type of the five selected in the section on pathology.

The book is well printed and of convenient size. The authors are to be congratulated on the success of their undertaking.

*Rôle de la constitution dans les maladies infectieuses des enfants*  
 By Hanna Hirsfeld 12°, paper, 152 pp, with  
 20 illustrations Paris: Masson et Cie, 1939 70c

Resistance to the specific infectious diseases varies markedly according to age, environment and, apparently, sundry other conditions. Racial immunities, relative at least, or, conversely, racial susceptibilities seem often enough conspicuous. Dr Hirsfeld believes, from the study of these together with the study of resistance in certain families and moreover, in plants and animals, that the factor of heredity is of very considerable weight. The transmission of resistance follows Mendelian laws, passing by way of a recessive gene. This is an interesting discussion, but in haphazard human breeding it seems to be of comparatively small practical importance.

*Heart Failure* By Arthur M. Fishberg, MD Second  
 edition thoroughly revised 8°, cloth, 829 pp, with 25  
 illustrations Philadelphia: Lea and Febiger, 1940 \$8.50

The first edition of this book appeared in 1937. In less than two years the entire edition was exhausted. The success of this volume is no accident, since the trend of modern medicine is toward a pathologicophysiology approach. The twentieth century physician is not so much concerned with "what happened," as with the "why" and "how." The contributions of the present era are more

expository than descriptive, the classic descriptions of disease being of the period that has passed.

Dr Fishberg has limited his subject to a minute field in medicine, and proceeds to expound all the processes involved. Yet a wide range of subjects is embraced: cardiac output, velocity of blood flow, arterial and venous pressure and pulse, and dyspnea, to mention only a few. It was once said that he who masters the subject of syphilis will know practically all medicine, for it simulates many diseases. The same thing is true of practically any disease. If one is to master all the pathologicophysiology processes involved in any one disease, he will have covered a great many of the fundamental sciences in medicine. Heart failure is a good illustration of this adage, even though the final word has not been said in a great many of these processes.

This new edition has all the merits of the first one, with the advantage of having been revised and having had the literature brought up to date. This book has already made a place for itself in the literature of cardiology, and is recommended highly to the student of medicine who is not satisfied with a description of disease but wants to get a peep behind the scenes.

*Digest of Laws and Regulations Relating to the Prevention and Control of Syphilis and Gonorrhea in the Forty Eight States and the District of Columbia* Compiled under the direction of Bascom Johnson, A.B., LL.B. 8°, cloth, 438 pp New York. Published and distributed by The American Social Hygiene Association, Incorporated, with the co-operation of The United States Public Health Service, 1940 \$5.00

This essential text for all persons working in the field of public health is arranged by states, which means a subdivision into forty nine chapters, thus making it very difficult to obtain information on a definite point. It could be greatly improved by the addition of a comprehensive index of subjects.

*Plague on Us* By Geddes Smith, M.D. 8°, cloth, 365 pp, with 14 illustrations, and 10 charts New York: The Commonwealth Fund, 1941 \$3.00

This is an excellent book of a semipopular type, based on sound scientific information. The author, associated with the Commonwealth Fund in New York City, has long been active in plague and the general subject of public health. His book covers briefly the entire history of plagues of various types, especially the well known plagues of the middle ages and those associated with definite diseases such as yellow fever, influenza, amebic dysentery, malaria and typhoid fever. Each chapter is written in a pleasant style, with enough slang to make a book of popular appeal. On the other hand, every sentence has been carefully weighed by the author. Sources of his material are given, with numerous references to the literature and splendid illustrations. The illustrations form one of the finest parts of the book, for they have been chosen with great care and bring out historical episodes in man's fight against epidemic disease. This book should be rated in the highest class of popularized medical literature, and it should have a wide appeal, not only to the public but to the more thoughtful person in the medical profession. Accurate and factual, the story, nevertheless, is invigorated by the style of a novelist, and

at once the old cliché comes to mind that "truth is stranger than fiction."

*Multiple Human Births: Twins, triplets, quadruplets and quintuplets.* By Horatio Hackett Newman, Ph.D., Sc.D. 8°, cloth, 214 pp., with 24 illustrations. New York: Doubleday, Doran and Company, Incorporated, 1940. \$2.50.

The distinguished author of this book records a special study of twins and supertwins made over a period of twenty-five years. It is written expressly for the general reader, with admirable success as to style and to human interest. Much of the material goes back to discussions of the heredity-environment problem at a round-table meeting attended by Professor Frank N. Freeman, an educational psychologist, Professor Karl J. Holzinger, an educational statistician, and the writer, a specialist in the biology of twins.

The author begins his book with a consideration of facts, fancies, fallacies and fiction about twins and then leads the reader to an understanding of the causes, varieties, psychology, intelligence and personality traits of twins. The closing chapters deal illuminatingly with the question of twins and the heredity-environment problem. The entire book is handled in a strictly scientific manner. The author concludes that much remains to be done on this extremely complex problem, although he has been successful in untangling some of the threads in that very intricate mesh that constitutes the organism we call man. Every library, general and special, should find a place for this intensely interesting book on its shelves.

*Psychiatry for the Curious.* By George H. Preston, M.D. 8°, cloth, 148 pp., with 17 sketches. New York: Farrar and Rinehart, Incorporated, 1940. \$1.50.

This clear, concise and amusingly written book will undoubtedly prove to be a useful addition to the class of medical literature that physicians can safely recommend to literate laymen; in fact, some psychiatrists could probably read it with profit. After six introductory chapters dealing in simple terms with psychopathology, the author covers briefly but adequately the major psychiatric syndromes and concludes with a short chapter on treatment. Among the most satisfying features of the book are the technically crude but extremely effective line drawings by the author at the beginning of each chapter; they possess a wild Thurberesque quality that not only sets the tone for each chapter but adds a whimsical touch too infrequently encountered in psychiatric literature, lay or professional.

*Legal Guide for American Hospitals: Prepared in collaboration with the Council on Government Relations of the American Hospital Association.* By Emanuel Hayt, LL.B., and Lillian R. Hayt, M.A., J.D. 8°, cloth, 608 pp. New York: Hospital Textbook Company, 1940. \$5.00.

This book is exactly what its title suggests, and is an invaluable reference book for the hospital administrator or trustee. It not only sets forth the general principles governing the formation, organization and the activities of various hospital departments but also cites legal examples that well illustrate the basic principles. Although a fairly large volume, it is divided into chapters relating to the different subjects, which are not unduly lengthy; in fact they are admirably condensed and yet cover all the points involved. It is by far the best legal reference book for hospitals that has been published to date.

*Psychiatric Social Work.* By Lois Meredith French. 8°, cloth, 344 pp. New York: The Commonwealth Fund, 1940. \$2.25.

For many years the need for such a book as this has been recognized by social workers, psychiatrists, educators and others interested in this field. The author's presentation of the origin, growth, definition, analysis and interpretation of the work, as well as its function in hospitals, clinics, educational institutions and public-health organizations, appears to give a complete description of all psychiatric social work. It is regrettable that the book does not fulfill its objectives in all respects. For example, mental deficiency is a great and growing problem and is proving to be a fertile field for psychiatric social work, but is entirely overlooked by the author. Likewise, clinics are described in detail, yet the Massachusetts traveling school clinics, which examine over nine thousand problem and retarded school children each year, are not mentioned.

The trends in social treatment over the past twenty years, present changes and developments and indications of trends for the future are outlined. The report of progress shows that the work of psychiatric social workers has gradually become more definite and clear cut. The training programs set up by schools of social work indicate the same tendency. Psychiatric social work has become definable in two different ways: either, "social work practised in relation to psychiatry," or "social work with emotional difficulties in any setting." The American Association of Psychiatric Social Workers affirms the former.

Although there is much material necessary to make this book a complete study of psychiatric social work, omissions are excusable when it is remembered that this is the first book of its kind. It is worthy of the attention of all who are a part of, or interested in, psychiatric social work.

*Science and Seizures: New light on epilepsy and migraine.* By William Gordon Lennox, M.D., Sc.D. (Hon.). 8°, cloth, 258 pp., with 10 illustrations. New York: Harper and Brothers, 1941. \$2.00.

The interest of the public in epilepsy has been growing markedly in the last few years. This growth is in large part due to the energy of the author of this book, who has been in the forefront of both investigation of the disease and promulgation of the measures to ameliorate the social status of sufferers from epilepsy. He is now president of the International League Against Epilepsy, vice-president and a very active member of the Laymen's League Against Epilepsy and secretary of the Harvard Epilepsy Commission. Dr. Lennox, moreover, has been active in the development of the new science of electroencephalography, a type of research that has thrown a great deal of light on the mechanism of epileptic seizures and particularly of the hereditary aspects of the disease. With this in mind, he has written a book for popular consumption based on a sound scientific knowledge of epilepsy, in addition to an unusual ability to state in clear language, easily understood by the layman, the somewhat complicated story of epilepsy as it is viewed today by the scientific worker. The book is essentially sound and can safely be put in the hands of any patient with this disease. Moreover, it should have a wide appeal to the public. Any profits that accrue from the sale of this book revert to the Laymen's League Against Epilepsy.

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## NONARTERIAL DISORDERS SIMULATING DISEASE OF THE PERIPHERAL ARTERIES\*

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BOSTON

THE clinician who suspects the presence of arterial disease in a patient's limb can usually make a positive diagnosis of such involvement. Occasionally, however, a disorder in some distant structure is responsible for the presenting symptoms, either through a direct action on the blood vessels of the extremity, or entirely independently of them. It is the purpose of this paper to call attention to the more frequent types of such distant lesions that cause difficulty in the differential diagnosis.

### DISORDERS SIMULATING CHRONIC ARTERIAL DISEASE

The chief chronic organic disorders of peripheral arteries are arteriosclerosis and thromboangiitis obliterans, whereas the vasospastic disorder known as "Raynaud's disease" is the most important functional derangement.

The diagnosis of organic arterial disease depends considerably on the evidence of the diminution in arterial blood flow, which has been summarized<sup>1</sup> as follows: muscle action is weak, and intermittent claudication may develop; the limb is abnormally cold; hypesthesia, hyperesthesia and spontaneous pain may be present; there is diminished resistance to injury, and ulceration may result from slight trauma; the toes and feet show blanching on elevation, and rubor on dependency; and the pulsation in the affected arteries is either slight or absent.

Raynaud's disease is characterized by spasmodic attacks of coldness, with blanching or cyanosis in the fingers and toes, on exposure to cold. The major vessels are not affected, and the major pulses remain normal. The etiology of this infirmity is uncertain, some authorities attributing

it to hyperactivity of the vasomotor system, others to a local vessel fault; but it will be here classified as a vascular disorder, from which other cases of vasospasm will be differentiated.

A great variety of conditions may resemble true arterial disease.

### *Arthritis*

The pain of spinal arthritis commonly radiates down the upper and lower extremities. Von Bechterew,<sup>2</sup> in 1899, pointed out that the pain of arthritis may be due to the pressure of inflammatory exudate on the spinal nerves or their roots. In 1916, Nathan<sup>3</sup> demonstrated, in experimentally produced arthritis, thickening of the vertebral bodies pressing on the spinal cord, and the infiltration of exudate in and about the vertebral articulations encroaching on the nerve roots or trunks in the intervertebral foramina. It is probably justifiable to assume that such lesions occur often in arthritic patients.<sup>4, 5</sup> This thesis is further strengthened by the amelioration of neuritic symptoms after the application of spinal traction.<sup>6</sup>

In arthritis of the cervical spine, the neuritic symptoms may resemble those of Raynaud's disease or of cervical rib disease.<sup>7</sup> Tingling of the fingers, often accompanied by hypesthesia and pallor, is apt to be the predominating symptom. In addition, poorly localized pain is usually present in and about the shoulder and in the entire extremity. These symptoms are often intensified by placing the limb in certain positions, which vary with the patient. An outstanding complaint is that the symptoms increase with recumbency and are intensified when the patient awakes in the morning.

Vascular disease may be further suspected because of coldness of the fingers and actual reduction in pulse volume (Fig. 1). The cervical nerves receive their sympathetic fibers beyond the inter-

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vertebral foramina; therefore, direct pressure on them or their roots cannot account for the vasospasm, but it may be a reflex from the joint irritation (Fig. 2). Dr. Thomas H. Peterson, in a personal communication, states that in such cases the application of head traction may cause a fall in the diastolic arterial pressure in the limb, with

in the cervical spine in the roentgenogram is, of course, significant.

CASE 1. A. T., a 40-year-old married woman, was referred for disagreeable prickling sensations in the fingers of both hands, associated with coldness and sweating. The onset was gradual in the early autumn and had lasted for 1 month prior to examination. The diagnosis of Raynaud's disease was considered, especially since two of the patient's sisters had disorders of this type. Further questioning elicited the fact that the prickling was present during the night, and was particularly troublesome when the patient awoke in the morning. She recalled no changes in the color of the hands. Likewise, there was no association of the attacks with exposure to hot or cold air or water.

Examination showed cold sweaty hands and fingers. There was no discoloration, deformity or trophic change, and sensation was grossly normal. Both radial pulses could be easily palpated, but the Pachon oscillometer showed a slightly diminished pulse expansion at the wrists, consistent with some vasoconstriction. Motion of the neck was full in all directions. Roentgenograms of the cervical spine showed a hypertrophic arthritis, with calcification of the intervertebral ligaments.

The patient received immediate benefit from diathermy treatment of the cervical spine. Recurrence of symptoms was expected, however, with any reactivation of the arthritis.

If arthritis attacks the lumbar spine, symptoms are experienced in the lower limbs, analogous to those described above. The pain does not often lie along the sciatic nerve, but is apter to be found in other regions of the limb. In the foot, it may be accompanied by hypesthesia and paresthesia, an association strongly suggestive of arterial insufficiency. More typical, however, is poorly localized pain in the thighs. This is ordinarily not diminished on activity, and occasionally its exacerbation on walking may be associated with cramps, which differ from those of true intermittent claudication in their location and lack of regularity. As in the upper extremity, vasoconstriction may be marked. It is noteworthy that the symptoms are by no means necessarily bilateral.

CASE 2. S. G., a 62-year-old tailor, complained of coldness and pain in the left lower leg. Fourteen years previously, he had an attack of severe pain in the left foot and ankle, necessitating bedrest for several weeks. Three years before, he had a recurrence of the pain, which disappeared after massage. Three months before the patient was seen, the pain again returned. It was described as a "drilling" or "pressing" in the left foot and ankle, and was initiated by standing or walking. Walking was indeed almost impossible, since the pain forced the patient to stop for a few minutes' rest about every 25 feet. The discomfort disappeared immediately on resting. He also described an additional, more constant pain throughout the thigh, which was increased on recumbency. The patient refused to stay in a supine position on the examining table, because it induced cramps in his left thigh. It was brought out that these cramps frequently occurred at night.

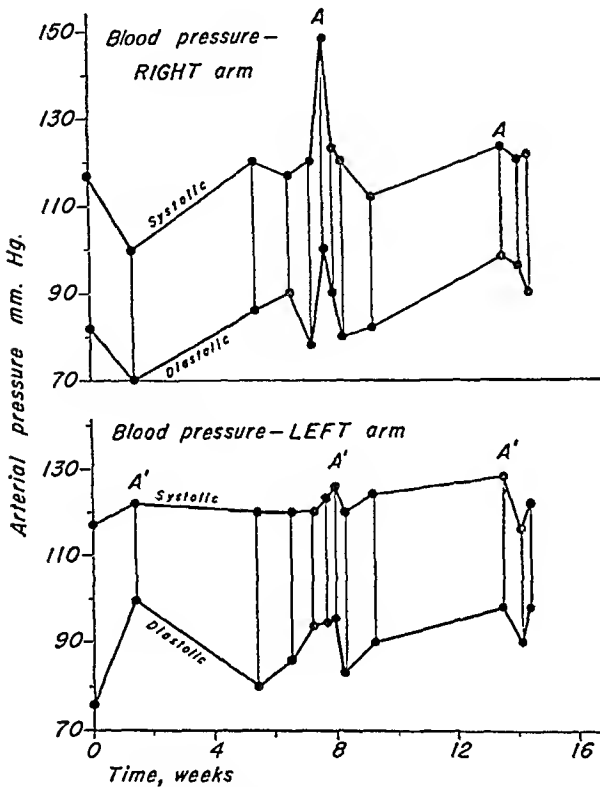


FIGURE 1. The Brachial Blood Pressure in a Patient with Cervical Arthritis. (Courtesy of Dr. Thomas H. Peterson.)

Pain radiating into the right upper limb occurred at A, and in the left limb at A'. The blood pressure was high on the affected side during the attacks of pain, presumably because of vasoconstriction in the distal parts of the limb.

a corresponding increase in the amplitude of the pulse.

Symptoms are not always present in the neck. Likewise, clinical examination may not reveal any abnormality there. Thus Turner and Oppenheimer,<sup>7</sup> in their reported group of 50 patients, most of whom, at least, were arthritic, found only 2 who complained of pain in the neck, and only 2 who had restriction of cervical motions. The history is nevertheless of extreme importance, inasmuch as the patients do not suffer most on exposure to cold air but, contrariwise, may be most uncomfortable in bed when the extremities are adequately warmed. The joints of the fingers may or may not show arthritic changes. The finding of either atrophic or hypertrophic changes

Examination showed coldness of both feet, with the surface temperature of the left foot  $3^{\circ}\text{C}$  below that of the right. There was no blanching on elevation, and no rubor on dependency. All the arterial pulsations were palpable, with the exception of that of the left posterior tibial artery. The Pachon oscillogram showed a diminished pulse amplitude, the reading of the right ankle being 25 units, that of the left 20 units. The spine showed a loss of the normal anterior convexity of the lumbar region with an extreme right dorsal, left lumbar scoliosis,

in severity, back exercises were instituted. After the ninth treatment, he felt greatly relieved, and diathermy was discontinued.

If the arthritis involves the joints of the limb, it is usually a simple matter to avoid its confusion with vascular disease. In cases of pain in the foot, for example, immobility on manipulation may point to involvement of the small joints of this

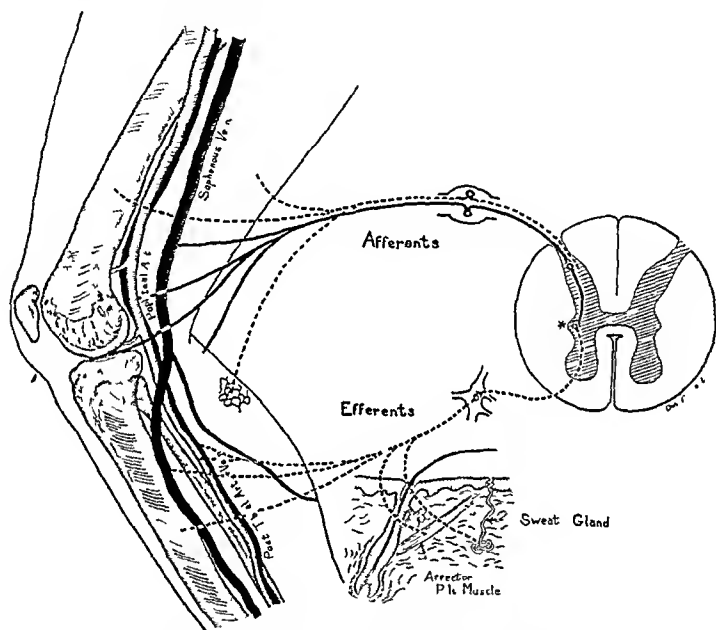


FIGURE 2 Pathways for Vascular Reflexes Originating in the Limb (modified after de Takats<sup>1</sup>)

Afferent impulses can arise in any of the tissues including bone joint skin artery and vein. The stimuli travel by way of the sensory fibers of the spinal nerves (solid line) to reach the cells of the intermediolateral column of the cord. These cells (\*) represent a 'final common path' of the sympathetic system since they receive impulses from all levels of the nervous system and send their processes outward to the sympathetic ganglia. Postganglionic fibers conduct the efferent impulses to the arteries and veins (constriction) as well as to the sweat glands and arrector pili muscles. Some sensory fibers of the spinal nerves (broken line) conduct afferent impulses from the skin or deep tissues and through an axon reflex give rise to the efferent response of vasodilatation in the capillaries of the extremity.

but good flexibility. X-ray examination showed prominent spurs at the margins of the lower dorsal and lumbar vertebrae, with calcific bridging of the 1st lumbar intervertebral space. The hip joint likewise showed hypertrophic changes.

The patient was placed on a high vitamin, low-carbohydrate diet, and diathermy treatment was given to his spine. The feet became warmer, and the pulses increased somewhat in amplitude. After four such applications, the patient could lie flat on his back without cramps in the thigh, and the symptoms on walking had diminished

part. Arthritis of the knee may cause pain radiating into the calf. Here one should recall that the pain of an arthritic knee is usually worse on arising, but diminishes with moderate use. Examination will show periarthritic thickening, with or without crepitus and pain on motion.

Decision is difficult when the pain is increased by walking, particularly if it is cramplike. This is perhaps seen oftener when the arthritis involves

the hip. As in spinal arthritis, this cramp is differentiated from that of true intermittent claudication by its irregularity in time and in degree of severity. Clinical examination may not demonstrate disability in the hip joint, but involvement of the more accessible joints points to the diagnosis, and the roentgenogram may be of great aid.

CASE 3. L.S., a 40-year-old housewife, was referred for pain in the lower extremities of 1 year's duration. The pain appeared in both ankles while the patient was walking, but it was less troublesome there than in the upper medial part of the left thigh, where it was cramp-like. The patient had to stop and rest because of the pain, but the distance traversed between rest periods varied from time to time and day to day.

Examination of the lower extremities showed strong pulsations in all the arteries. The saphenous veins were moderately dilated, and some valvular incompetence was manifest. There was a little loss of mobility in the feet, but no evidence of arthritis in the knees or back, or in the joints of the upper extremities. Extremes of hip motion reproduced the crampy pain in the left thigh. Roentgenograms of the hip joint showed hypertrophic changes. The patient's symptoms were attributed to the arthritis of the left hip, and improvement was obtained by treatment similar to that mentioned in the previous case.

### *Diseases of the Nervous System*

Lesions of any part of the nervous system, from the brain to the finer nerve branches, may mimic chronic arterial disease. As a well-known example, one may mention the cold and cyanotic extremities in the chronic stage of anterior poliomyelitis, and in the catatonic type of dementia praecox.

The simulation to arterial disease is frequently brought about independently of any known vascular change. In these cases, it may be especially confusing if trophic ulceration is present, since ulceration often has its origin in intrinsic vascular disease. Medical writers have unfortunately caused some confusion by using the term "mal perforans" for any perforating lesion of the foot or toe, regardless of the etiology. The presence or absence of sensitivity in such a lesion is, happily, an excellent guide to its true etiology. When the ulcer is of vascular origin, there is usually severe pain. The trophic ulcer of nervous origin, on the contrary, is usually located in a zone of hypesthesia or anesthesia. A determination of the neurologic state of the limb and the patient, on the one hand, and the vascular state, on the other, allows one to establish the correct diagnosis.

CASE 4. M.M. (Boston City Hospital No. 79470), a 39-year-old laborer, was first seen at the outpatient department of the hospital for a septic callus over the plantar surface of the left 5th metatarsal. Amputation of the 5th toe and head of the metatarsal was performed because of the presence of osteomyelitis.

Six months later, the patient developed an ulcer on the plantar surface of the left great toe (Fig. 3). The foot was cold, sweaty and cyanotic, findings that suggested an underlying vascular lesion; both the dorsalis pedis and posterior tibial pulses were normal, however. The plantar surface of the toe, including the base of the ulcer, was so anesthetic that the underlying bone, which was carious, could be probed without producing the slightest pain.

Further questioning revealed that the patient had fallen down the hold of a ship and injured the spine, 12 years previously. He was treated by a plaster cast, then by a



FIGURE 3. *Mal Perforans of the Great Toe.*

*In this patient (Case 4), the condition was associated with injury to the lumbar nerve roots following a compression fracture of the spine, but the peripheral arteries were normal. Carious bone was present in the floor of the ulcer. The fifth toe had previously been amputated for the same disorder.*

brace, for 2½ years. From that time on, he had no symptoms until the onset of the present illness. He admitted some dribbling of urine for 3 weeks prior to the last examination, but no rectal incontinence and no impotence.

X-ray examination showed an old compression fracture of the body of the 2nd lumbar vertebra, with bony union between it and the body of the 1st lumbar vertebra.

There was hypesthesia of the body on both sides below the distribution of the 1st lumbar nerves. The knee jerks were diminished on the right side, and the ankle jerks were absent. There was a positive Babinski reaction on the left side. A laminectomy was performed by Dr. Walter Wegner. There was demonstrated a considerable mass of scar tissue, both fibrous and bony, at the level of the 1st and 2nd lumbar vertebrae, involving some of the anterior and posterior roots of the cauda equina. The scar tissue was removed, some of the roots being unavoidably injured during this procedure. The symptoms gradually regressed after operation, and the ulceration of the foot healed after several months.

Peripheral neuritis of various forms may simulate arterial disease even when unaccompanied by ulceration. This is due in part to the presence of pain in the limbs, and in part to coldness incident to vasospasm. In this connection, Lewis and Pickering<sup>8</sup> state:

The chief cause of lowered skin temperature after mixed nerve lesions is loss of the fibers belonging to the posterior root system. While it is probable that this loss is effected chiefly through the disappearance of the sensory axon reflex [normal vasodilatation mechanism], we are unable to exclude the possibility

that loss of vasodilator impulses passing from the cord by posterior root fibers may also play a part (See Fig 2)

Dole and Morison,<sup>9</sup> however, could find no evidence for the existence of the second mechanism mentioned

CASE 5 L J, a 42-year-old jeweler, was referred for cramps in the feet and calves of 8 years' duration. The cramps came mostly at the close of any day that required much standing. On some occasions, they appeared while the patient was standing and could be relieved by walking; whereas at other times, they came on only after traversing a block or two. For 3 years before consultation, the patient was troubled by this symptom at night, which necessitated his getting out of bed for a few seconds, when the cramps disappeared. The patient's malady was worse in the 3 weeks prior to the examination, a fact attributed to a temporary increase in work. Additional evidence was secured that the patient had been a fairly hard drinker for many years. During the month preceding examination, he had taken several drinks a day and finally had been confined to his home for several days because of alcoholism. He had become extremely apprehensive and had entertained some delusions. His diet was admittedly poor, with a minimum of fresh vegetables. He had begun smoking at the age of 16 and, at the time of examination, smoked ten to fifteen small cigars a day. Chronic otitis media and mastoiditis were present and possibly operated as additional toxic factors.

Examination showed moist, cold feet. There was no discoloration and no blanching on elevation. The femoral and popliteal pulses were excellent. Although neither dorsalis-pedis pulsation could be felt, the posterior tibial pulses were of excellent quality. The oscillometer showed small but equal pulse expansions at the ankles. There was some superficial tenderness on the dorsum of the feet and a little extensor weakness. Both feet were in moderate pronation.

It was believed that the coldness and sweating represented vasomotor symptoms due to an alcoholic neuritis or, possibly, to the patient's smoking. Relief from the cramps was obtained by an increase in vitamin intake, a reduction in smoking and measures directed to pronation of the feet, namely, the use of orthopedic heels and foot exercises.

So-called "ganglionitis" and "radiculitis" are troublesome variants of peripheral neuritis.<sup>4, 6</sup> The presenting symptom usually is intractable pain in the foot or leg, which on close questioning is characteristic of a hyperesthesia. The symptoms vary according to whether the posterior or anterior roots, or both, are involved. Examination may disclose areas of hyperesthesia or anesthesia, with muscle weakness and abnormal deep reflexes. The majority of cases occur in the lower extremity.

CASE 6 C H, a 57-year-old housewife, was referred because of pain and coldness of the right foot, and cramps of the right calf, of several years' duration. There was fairly constant pain and blanching in the 2nd toe. The remainder of the foot was cold and blanched spasmodically especially in cold weather. The patient avoided walking because of heaviness in the leg. This symptom

was usually not accompanied by cramps, which were apt to appear at night. The patient believed that at least some of her symptoms dated back 39 years to an attack of herpes zoster that had involved the right lumbar region.

Examination of the lower limbs showed normal cutaneous color in all positions. Both feet were cold however, the right more than the left. The right dorsalis-pedis pulse could not be felt but its absence was apparently adequately compensated for by a palpable peroneal and a large posterior tibial pulse. The left dorsalis pedis and posterior tibial pulses were forceful. Oscillometric examination showed good arterial pressure and pulse amplitude at both ankles.

In contrast to its normal vascular status the limb showed abnormal neurologic findings. The patient was transferred to the care of Dr Tracy J Putnam, whose findings were as follows:

Motor power was good in both legs and both feet, the right ankle jerk was more active than the left, however, and there was a suggestion of clonus on the right. The Babinski reaction was negative on both sides. There was hyperesthesia over an area of the dorsum of the right foot centering around the 2nd toe and plantar surface of the 2nd and 3rd toes. The hyperesthesia was most marked to pinprick. There was a loss of vibratory sense in the ankle but no loss of position sense. There was no tenderness of the sciatic nerve, but there was tenderness of the lower spine. Small scars in the mid line were suggestive of an old herpetic eruption.

It seems to me that the diagnosis must be a chronic progressive neuritis. In view of the old history of pain, the long-continued subjective heaviness of the right leg and the hyperesthesia this must have affected the whole sciatic nerve to some extent, but is most intense in the peroneal branch. I believe that it is a result of the old herpes.

According to Dr Putnam's suggestion, the patient was given deep x-ray therapy over the roots of the sciatic nerve. After ten treatments, she experienced complete relief from her symptoms.

A more puzzling interplay of neurologic and vascular symptoms is present in the syndrome of causalgia, resulting from injuries to the large nerves, especially the median and sciatic. The symptoms, which are disagreeable and disabling, consist in extreme hyperesthesia, with coldness, cyanosis and sweating.<sup>10, 12</sup> Similar disorders of less severe degree may follow almost any injury in any part of the extremity. Such cases following a fracture, sprain, puncture wound or mild infection have been described by several authors.<sup>11-13</sup> As emphasized by de Takats,<sup>17</sup> this category of reflex dystrophy of the extremities includes syndromes designated as reflex vasoconstriction, traumatic osteoporosis, traumatic arthritis and so forth. Common to all such disorders is an irritation of a sensory nerve or its endings, which sets up reflexes mediated by the sympathetic fibers with an effector response in the blood vessels (Fig 2). The sweat glands and arrector pili muscles may also react, thus giving rise to locally



excessive sweating and to an exaggerated pilomotor ("goose-flesh") reaction. Homans<sup>18</sup> adds a theory that some of the sensory changes are due to the interference with the nutrition of the larger nerve trunks caused by the reflex vasoconstriction of their nutrient arteries.

When a diminution in blood flow results from such disorders, it becomes necessary to rule out organic obstruction of the arteries, which indeed may have been produced by the primary injury to the limb. The decisive data are obtained by

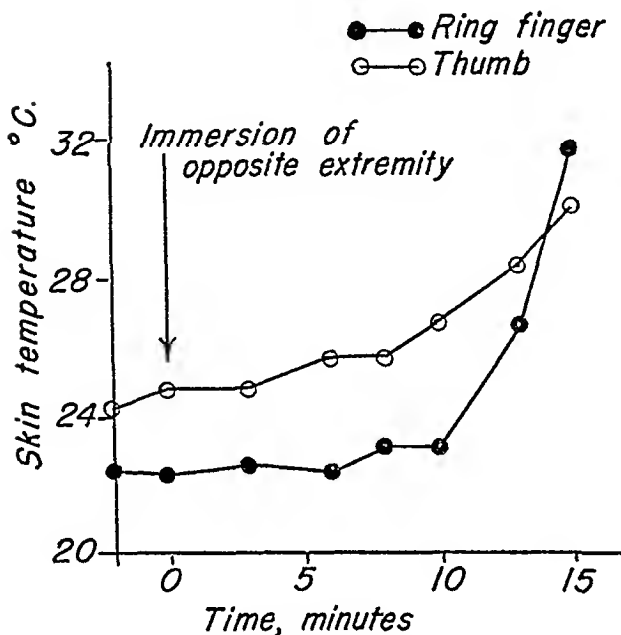


FIGURE 4. *A Vasodilatation Test in a Patient (Case 7) with Vasospasm Secondary to a Scar Neuroma of the Ring Finger.*

*Immersion of the opposite extremity in warm water resulted in a pronounced vasodilatation of the affected finger and a rise in the skin temperature to a level at least as high as that of the normal first digit. The test established that the diminution in blood flow was reflex in nature and ruled out organic disease of the peripheral arteries.*

inhibiting the vasomotor control of the vessels.<sup>19</sup> The uninvolved extremities may be immersed in hot water at 43°C. (Landis-Gibbon test), or spinal anesthesia may be induced for the lower extremities and paravertebral sympathetic anesthesia for the upper extremities. If the diminution in blood flow depends entirely on vasospasm, without any organic vascular obstruction, the sympathetic inhibition allows a considerable increase in blood flow to occur. This effect can be measured by determining the skin temperature or the oscillometric index of pulse expansion, before and after the test (Fig. 4).

When one is dealing with a reflex effect, relief will be obtained if the irritable focus can be ex-

cised, as in the case described below, or if the reflex can be interrupted, as by sympathetic ganglionectomy.

CASE 7. M. A. H., a 29-year-old factory worker, was seen for pain and coldness of the right ring finger. Seven months prior to consultation, a sliver of steel had passed under the nail, and the finger had become infected. The finger tip was incised under procaine block at the base of the digit, and under general anesthesia on two more occasions. Immediately after the last incision, the finger became white, cold and painful. The pain was constant, necessitating sedation at night. The slightest touch of any part of the finger resulted in intense pain, and the symptoms were likewise increased on exposure of the hand to cold. The patient was not working. He was depressed mentally, and had lost 18 pounds.

Examination showed the finger to be blanched from base to tip. Both this digit and the little finger were strikingly cold, the temperature being 2.5°C. below that of the other digits. An exquisitely tender scar, 8 mm. long, was present on the tip of the injured finger, but the hyperesthesia extended beyond this zone onto both surfaces of the finger to its base. The pulses at the wrist were normal to palpation and by oscillometric measurement.

The obvious marked diminution in local blood flow brought up the possibility that the digital arteries had been thrombosed during the infection, or by the digital nerve block. To determine whether the vessels were thus obstructed, the cutaneous temperature of the fingers of the right hand was measured before and after immersion of the normal left hand and forearm in hot water. Adequate vasodilatation resulted (Fig. 4). The digital arteries were therefore not organically blocked but, on the contrary, were in a state of vasoconstriction, apparently secondary to the tender scar of the finger tip.

Excision of the scar resulted in the complete disappearance of the disorder.

### Phlebitis

It is known that phlebitis is often accompanied by vasospasm, manifest by small pulses and coldness in the extremity, and may thus resemble a primary arterial disorder.<sup>20</sup> It is quite evident that, from the standpoint of the mechanism of this vasospasm, phlebitis is, like the other conditions considered above, one particular source of sensory irritation that is adequate to set off vasoconstrictor responses.

In a previous report,<sup>20</sup> it was emphasized that the arteries are but one of several structures in the limb that, because they receive sympathetic innervation, are all equally liable to react to venous irritation. These structures include the veins, the sweat glands and the arrector pili muscles (Fig. 2). Therefore, if arteriospasm is present, it may be associated with sweating of the cold extremity and an abnormally active pilomotor reflex ("goose-flesh").

Severe arteriospasm giving loss of the major pulses may occur, but is much less common than minor degrees of vasoconstriction. To establish

the true nature of the disturbance, one must look for the typical tender induration of the phlebitic vein, and the cyanosis and edema on standing. Phlebitis may further be suspected as the cause of the diminished arterial flow if there are accompanying sweating and increased pilomotor response. The latter reflex is easily tested by pinching the skin of the extremity, or by touching it with a cold object. Finally, one should be able to demonstrate that the blood flow can be increased, after sympathetic release, by one of the methods described in the preceding section.

CASE 8. M. P., a 40-year-old married schoolteacher, was referred for pain and coldness of the right foot, following a fracture of the 5th metatarsal bone. These symptoms were constant, and increased on standing or walking, when they were accompanied by cyanosis and edema of the limb. For some months prior to the accident, the patient had noticed cramps, which appeared during the night but not while she was walking. With this history in mind, and because no pulsations could be made out in the pedal arteries, her local doctor had suspected arterial disease and had treated the patient by injections of a pancreatic extract (Depropanex). At the end of 2 weeks' bedrest, the swelling diminished but the extremity was still painful and cold.

On examination, the right calf showed 13 cm of atrophy. There were moderate cyanosis and coldness in the lower leg, foot and toes. The toes blanched slightly on elevation. There was no excessive sweating, but the pilomotor response was exaggerated. The femoral and popliteal pulses were of good quality, and although the pulsation of the dorsalis pedis artery could not be felt, that of the posterior tibial artery was fair. On the unaffected left side, the pulsations were approximately the same, with a nonpalpable dorsalis pedis but a slightly larger posterior tibial pulse. Moderate edema was present on the medial side of the affected ankle, and a tender thickening could be felt along 12 cm of the course of the saphenous vein in the lower calf. There was but minimal tenderness over the 5th metatarsal bone, and an x-ray film showed good healing of the fracture.

The nocturnal cramps preceding the injury were presumed to be due to a varicose widening of the saphenous vein. This was borne out by the discovery of a dilated vein at operation. The tenderness over a segment of the vein, in addition to the cyanosis and edema, pointed to a phlebitis that might have started in the deep veins following the primary trauma, with subsequent extension to the saphenous vein. The coldness and exaggerated pilomotor response were consistent with a sympathetic reaction from the phlebitic vein.

A ligation of the saphenous vein was performed under spinal anesthesia. Skin temperature and oscillometric readings showed adequate vasodilatation after the anesthesia and operation, a finding indicating that there was no organic obstruction of the arteries. Conversely, the experiment strengthened the conclusion that the coldness of the extremity was due to a vasospasm, presumably secondary to the phlebitis.

The symptoms quickly diminished. Small areas of thrombophlebitis appeared in the superficial veins of the thigh. Radiant heat and diathermy were given to the limb, and active exercises were started. On discharge, the same treatment was continued by the family physician, and the symptoms regressed satisfactorily.

### *Cervical Rib, Anomalies of the First Thoracic Rib and the Scalenus Syndrome*

Although cervical rib is usually included in a classification of vascular disease, it is more properly considered as a condition that simulates primary arterial disease.

The symptoms can be both neurologic<sup>21</sup> and vascular, and may be constant or spasmodic. The patient usually complains of numbness and tingling in the limb, especially along the medial side of the forearm and hand and in the more medial fingers. Muscular weakness and wasting may occur in the hypthenar muscles or, less commonly, in the thenar group. True vascular symptoms are infrequent. They include episodes of blanching or cyanosis of one or more fingers or of the entire hand. Both sets of symptoms occur, especially in relation to muscular effort or to changes in position of the neck or the extremity. Exposure to cold may inconstantly initiate an attack. The blood pressure may be lowered on the affected side, and the radial pulse may be small and, very rarely, obliterated. Pain may be felt in the neck, radiating into the shoulder. If the rib is large, there may be a visible elevation. In some cases, the subclavian pulsation is more prominent than normal; this happens most frequently when the rudimentary rib belongs to the first thoracic segment.<sup>22</sup>

It is apparent that the neurologic symptoms are caused by the impingement of the lower trunk of the brachial plexus on the cervical rib<sup>21-23</sup> (Fig 5). Todd<sup>25</sup> and others<sup>26-27</sup> believe that vascular symptoms, when present, are caused by the concomitant irritation of the sympathetic fibers in the trunk, whereas Lewis and Pickering<sup>28</sup> and others<sup>29</sup> conclude that these symptoms depend on actual contact of the rib and the subclavian artery. Murphy<sup>30</sup> suggested that the scalenus anterior muscle, placed in front of the artery and nerve, plays a role in the production of symptoms by pressing these structures against the rib. This thesis was reaffirmed by Adson and Coffey.<sup>31</sup>

It is worth remembering that an abnormal first thoracic rib may give rise to symptoms identical with those of a cervical rib.<sup>22-23</sup> Finally, there is a much larger group of patients, with the signs of cervical rib, who show no bony anomalies.<sup>34-37</sup> Here, as in cervical rib, symptoms are apparently caused by injury to the lower trunk of the brachial plexus as its component from the first or first and second thoracic nerves arches upward and outward over the first rib to gain the limb (Fig 5). An exaggeration of the downward slope of the shoulder (especially pronounced in women) may initiate, or at least aggravate, this irritation. Niff

CASE 11. A 46-year-old man entered the hospital because of pulmonary embolism resulting from a phlebitis in the deep veins of the right leg. Within the next two weeks, the phlebitis ascended to the right femoral and iliac veins. This was followed by sudden pain in the left groin and inability to move the extremity. The left leg was cold, dry and anesthetic to the knee. Above, it was hyperesthetic. Before this episode, all the pulses of the leg had been palpated and found to be normal, but shortly thereafter no pulsation could be detected in any of the vessels from the femoral artery downward.

The symptoms disappeared and the pulsation returned in full force within 45 minutes after the application of heat.\* Induration of the left femoral vein was then apparent, and dilated superficial veins were visible in the left flank.

### *Disease of the Central Nervous System*

It has already been shown how diseases of the nervous system, both central and peripheral, may simulate chronic arterial disorders. The following case report is considered of particular interest, since an acute spasm of a major artery was induced by an intermittent disorder of the brain. It is possible that the cerebral cortex was involved in this reaction, since reported experiments indicate that the central and precentral areas of the frontal lobe are concerned in vasomotor control.<sup>39</sup> Peet and Kahn<sup>40</sup> report syndromes similar to Raynaud's disease that are incident to cerebral lesions, and refer as well to examples of the loss of a peripheral pulse during operative manipulation of the brain.

CASE 12.<sup>†</sup> J. J. (Boston City Hospital No. 800477), a 34-year-old woman, 19 days after a nephrolithotomy, suffered a sudden attack of transient numbness and weakness of the entire left side of the body, with a persistent right homonymous hemianopsia. Because of a previous history of rheumatic heart disease, this incident was ascribed to a cerebral thrombosis or embolism. One week later, the patient was seized with a sudden knifelike pain in the left groin. The limb was numb, palsied and cold, and the resemblance to arterial embolism was further increased by the absence of the femoral pulse. Operative exploration revealed a tightly contracted femoral artery, the pulsation of which, however, returned when it was stripped from its sheath. No embolus was found on incising the artery, and following operation the pulses returned in the extremity.

I saw the patient through the kindness of Dr. Tracy J. Putnam, to whose service she was transferred. Determination of the vascular status of the lower extremities showed small but probably normal pulsations; those on the left side were only slightly weaker than those on the right. The variation was of a magnitude often seen in normal extremities.

During the remainder of her hospital stay, the patient suffered attacks of probable cardiac asthma associated with occasional incidents of numbness and weakness of the left side of the body. In some of these attacks, the pulses of the lower leg disappeared and the retinal arterioles be-

came constricted. A similar attack, of greater severity, was induced by an intravenous injection of Ergobasine. Again the left femoral pulse disappeared, and the retinal vessels were seen to be constricted. The symptoms gradually wore off after the inhalation of carbon dioxide and oxygen.

Although certain aspects of the case pointed to the presence of hysteria, at least as a complicating factor, the consensus was that in the spontaneous episodes the patient had suffered from a cerebral and ophthalmic arteriospasm, which was associated with a spasm of the vessels of the left lower extremity. It was thought that this process had been repeated during the induced attack.

### SUMMARY

Chronic disease of the peripheral arteries, as well as acute thrombosis and embolism, may be simulated by a great number of disorders in the other tissues of the extremities or in quite distant organs. The mechanisms whereby the confusing symptoms are produced are discussed, and several case reports are cited to illustrate the methods of differential diagnosis. These cases include arthritis of the cervical and lumbar spine and of the hip joint, a cauda-equina lesion from an old compression fracture of a lumbar vertebra, ganglionitis, peripheral neuritis, scar neuroma, phlebitis, cervical rib and the postirradiation state. Peripheral arterial embolism was suspected in a patient with phlebitis and in one with probable cerebral arteriospasm. Doubtless several other diseases could have been represented.

It is apparent that a precisely detailed history usually gives the clue to the correct diagnosis. One must also attend to the general examination and evaluate carefully the condition of all tissues of the limb. Thus, in addition to the condition of the vascular system, the examiner must determine the cutaneous, neurologic, articular, osseous and muscular status. If arterial inadequacy is shown to exist, he must discover whether it is due to organic disease or to vasospasm secondary to some other disorder.

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\*If the condition had been true arterial embolism, local heating might have induced gangrene.

<sup>†</sup>This case is presented with the kind permission of Drs. I. J. Walker and S. J. G. Nowak, who reported it at a meeting of the Boston Surgical Society on February 3, 1936.

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## WHAT SENSIBLE LIVING AND NATURAL RECOVERY CAN DO FOR A CARDIAC PATIENT\*

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IN THESE days of high-pressure sales of medicines and the introduction of new surgical procedures, it is well to pause a bit and consider what may be accomplished by natural processes of healing and by sensible attention to the details of daily life. This observation applies to much of the field of internal medicine and especially to cardiac patients, most particularly those with rheumatic and coronary heart disease.

Much too often, recovery from a serious cardiac ailment is credited to a particular form of therapy, whether oral medication or surgical intervention. Follow-up studies have shown in many cases not only that recovery from an acute cardiac illness has taken place without special therapy, but also that these patients have lived useful lives for many years afterward. Such recovery and longevity, as will later be shown in illustrative case reports, occurs irrespective of the type of therapy instituted.

In a previous communication<sup>1</sup> attention was called to the fact that, although the prognosis

of heart disease in apparently serious and grave cardiac states is often a difficult problem, one should recognize the fact that "functional recovery may be so complete that the ultimate prognosis is good for many years after."

Although one may encounter a patient with what appears to be a mild heart attack who unexpectedly dies, we have seen the reverse in many cases—that is, very seriously ill patients who not only make an immediate recovery but are able to carry on their occupations, with some limitations, for many years. The age of the patient and the type of cardiac disability may play little or no role in the ultimate recovery.

Because of the importance of these considerations and of the frequency with which they are overlooked, we have assembled the records of 7 striking cases illustrative of a great many that we have seen. The types of heart trouble were: rheumatic heart disease with mitral stenosis (2 cases) and coronary-artery disease (5 cases). We have divided the patients into two groups: those experiencing a natural, that is, spontaneous, recovery (3 cases) and those in whom longevity was due, in part at least, to sensible living (4 cases). The term "natural recovery" refers to a return to

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health that we could not ascribe to any particular type of therapy.

CASE 1. J. E. K. was first seen in the Cardiac Clinic at the Massachusetts General Hospital in June, 1923, at the age of 13, when rheumatic heart disease with active rheumatic fever was found. In November, when there was no evidence of active (rheumatic) infection, he indulged in football without any ill effects. In April, 1924, because of what was thought to be a well-marked mitral stenosis, he was referred to the Peter Bent Brigham Hospital for valvotomy. Because of the presence of asthmatic bronchitis, operation was deferred. The patient returned to the Cardiac Clinic in 1931 for a check-up; x-ray examination showed marked prominence in the region of the pulmonary conus, with a normal transverse diameter of the heart. The electrocardiogram showed sinus arrhythmia at a rate of 70, with notched P waves in all leads. The findings were consistent with rheumatic heart disease. On October 11, 1934, the patient returned feeling well and without symptoms, and on April 30, 1940, at the age of 30, he again returned to the clinic. Examination showed a healthy appearing man. The blood pressure was 120/75. The pulse rate was 60 and regular. There was no abnormal pulse in the neck. The heart was normal in size. With the patient in the upright position, the only abnormality heard with the Bowles stethoscope was a very slight early diastolic blow at the lower end of the sternum and at the apex; this murmur could easily have been missed. With the bell at the apex, there was a rather loud 1st sound, and a 3rd sound with a very faint rumble following it. With the patient in the recumbent position, the mitral diastolic murmur was louder, with slight presystolic accentuation.

In this case there was no doubt about the presence of a relatively slight amount of mitral stenosis and of a very slight amount of aortic regurgitation, neither of which is apparently a serious burden to the heart itself. The "marked mitral stenosis" noted sixteen years previously was probably largely due to dilatation of the heart secondary to acute rheumatic infection. This patient has done very well, and is lucky to have escaped operation. The case illustrates the extreme care that one must exercise in making a correct diagnosis in the first place, and the natural tendency for the heart to do well for many years after the subsidence of active rheumatic infection.

CASE 2. G. B. D., an 84-year-old man, entered the Phillips House on February 4, 1938, seriously ill, with a story of recent angina pectoris decubitus. The patient, always hale and hearty until old age, had been bothered for several years by a series of illnesses and accidents, beginning about 10 years previously with an automobile accident. Five years before admission to the hospital, he developed glaucoma and cataracts, and 3 years before, swelling of the legs from varicose veins began. There had been no dyspnea or chest pain until the summer of 1937, when he began to have discomfort in the upper chest on both sides of the sternum on effort; this was relieved by rest. The severity of the attacks gradually increased during the fall and winter. Three weeks prior to entry, the patient had been awakened at night by this same ache, which recurred through that night and at intervals on later nights.

He had rested, but not in bed. Examination showed an elderly man, moderately ill, with normal blood pressure (145/80) and pulse rate (60). The heart was enlarged, with a total transverse diameter, by teleroentgenogram, of 17.5 cm. and a chest diameter of 31.0 cm. The electrocardiogram showed auricular premature beats with T<sub>1</sub> upright, T<sub>2</sub> low and T<sub>3</sub> inverted; there was moderate left-axis deviation, a PR interval of 0.20 second, and a normal Lead 4. A gastrointestinal x-ray series was normal.

Because this patient was already improving, without drugs, during the first few days in the hospital, no therapy except rest was prescribed. He improved steadily; in 2 weeks he was able to walk upstairs without symptoms, which he had not been able to do for weeks before, and not long thereafter he returned home free of symptoms *and without medicine*, much to the surprise of himself and of his family and friends.

In June, 1939, a close friend reported that the patient had been well after his return home in the winter of 1938 until the late winter of 1939, when he had a recurrence of his angina pectoris decubitus just like that of the previous year, which again cleared under the same therapy—rest without medicine, this time at home. In the summer of 1940, the patient was reported to be in good condition, even being able to attend evening meetings.

This case illustrates spontaneous recovery from severe coronary insufficiency—probably secondary to coronary thrombosis without infarction—twice at an advanced age. Rest, without drugs, doubtless helped in this recovery. The trouble with the eyes (glaucoma and cataracts) and with the legs (varicose veins) had restricted the patient's activities considerably, which may have prevented earlier symptoms of cardiac distress.

CASE 3. F. J., a stout, 61-year-old banker, in 1935, while sitting in a chair swallowing the first mouthful of a meal, fell unconscious without warning. The syncope lasted a few seconds. The patient had two similar spells in the next 2 days. He was then put to bed for 6 weeks, and reduced his weight from 246 to 226 pounds. An electrocardiogram showed right bundle-branch block but a normal PR interval. Two years later, in August, 1937, the patient fainted again, and thereafter was all right until October, when he began to have frequent attacks of faint spells and syncope. Despite much classic therapy, he continued to do very poorly, and was constantly threatened and actually affected by what was definitely proved to be Adams-Stokes attacks—the electrocardiogram during an attack showed a standstill of the ventricles, with a gradual return through partial grades of block to normal PR intervals. When he was at his worst, in March, 1938, the patient was having several attacks of unconsciousness daily. Physical examination showed no abnormalities, except for moderate obesity, a slight to moderate systolic murmur at the aortic valve area and at the cardiac apex, and occasionally an intermittent pulse, at a heart rate of 84. An electrocardiogram showed normal rhythm at a rate of 60 to 65, with right bundle-branch block and normal PR intervals. X-ray examination showed a full-sized heart, with a somewhat dense aorta.

The patient continued in a precarious state despite the use of atropine sulfate, nitroglycerin, ephedrine and injections of epinephrine hydrochloride intramuscularly—all of which did, however, undoubtedly help him tem-

porarily—during the next year. Finally, because of a critical sinoauricular heart rate of about 75, above which partial block and Adams-Stokes attacks occurred the administration of digitalis was advised. Because of a previous unfavorable experience with digitalis, Urganin was given, and under its influence, in addition to that of adrenalin, he rapidly improved and during the next year and a half was in surprisingly good health, completely free from any attacks of Adams-Stokes syndrome.

Physical examination in November, 1940, showed moderate hypertension (200/90), a moderately enlarged heart with harsh aortic and moderate apical systolic murmurs and no evidence of congestive failure. On fluoroscopic examination, there was moderate enlargement of the heart, with clear lungs. The electrocardiogram showed complete auriculoventricular block, with an auricular rate of 85, a ventricular rate of 40 and bundle branch block as before. The patient had reduced his weight to 216 pounds, and was quite active again, having resumed his regular work, though not intensely, at the age of 66 years.

This patient showed a hopeful recovery from partial auriculoventricular block with Adams-Stokes syndrome. The transition to complete heart block was doubtless spontaneous and accounts more for his present state of good health than the drug therapy does. However, it is probable that the drugs helped him over a critical period. Although his duration of life is uncertain, it is hoped that he may continue in his present fair state of health for some years to come. We have encountered similar patients who have survived for ten years or more after the establishment of complete heart block.

The effect of sensible living, not only on the well-being but also on the longevity of the patient, is clearly demonstrated in the following group of cases. To prescribe drugs and to advise certain surgical procedures in many cases of heart disease are not only advisable but at times essential and useful. However, one should define to his patients, clearly and forcibly, the importance of personal readjustment to individual needs. Each case has to be worked out by itself. Often the patients themselves can determine their optimum mode of living, not only from the viewpoint of comfort, but also from that of earning a livelihood.

**CASE 4.** A E, an 82-year-old man, was seen in February, 1937, with cardiovascular limitation, both in the form of angina pectoris, helped at first by nitroglycerin and in the form of congestive failure, which was greatly helped by digitalis. The patient suffered from progressive loss of vision, which began in 1910 and resulted in practically complete blindness in 1922, when glaucoma manifested itself; he continued to be active thereafter, however. In 1924, an electrocardiogram showed intraventricular block. The blood pressure was 170/110. The patient had dyspnea when he hurried, but his blindness prevented him from walking fast enough to cause much trouble with the circulation. In 1925 he developed angina pectoris and the diagnosis of hypertensive heart disease was added to the previous ones. In 1926, definite evidence of

congestive heart failure appeared, and the patient felt better when digitalis therapy was instituted. In 1927, he was given hypertonic salt solution intravenously, and this procedure was followed by an attack of coronary thrombosis. In the 10-year period following this attack, he suffered a good deal of cardiovascular limitation caused by angina pectoris, which was relieved by nitroglycerin, and by congestive failure, which was helped very much by digitalis.

The patient gradually learned how to improve his health by rest breathing exercises and a careful diet. By this regime, his symptoms largely subsided in the course of years, so that he had almost no angina pectoris and little or no dyspnea although it is true that he walked very slowly. He continued actively at work throughout the years, going to his office daily and resting almost completely in bed over week ends. On one occasion in the fall of 1937, he was referred to the Baker Memorial Hospital for rest on account of an increase in coronary insufficiency; this treatment resulted in considerable improvement. In February, 1940, he contracted bronchopneumonia and was admitted to the hospital. Although he seemed to weather the infection, he became very weak and died from a fresh coronary thrombosis 10 days after entry.

**Autopsy.** The heart weighed 500 gm. There was a mural thrombus in the left ventricle, with acute coronary thrombosis in the left descending branch, as well as a healed cardiac infarction, generalized atherosclerosis and marked coronary sclerosis.

Here was an ingenious and wise man who taught his doctors how Nature, common sense, the affliction of blindness and personal experimenting aided longevity while he continued a useful life.

**CASE 5.** M P, a 43-year-old salesman, underwent a total thyroidectomy in January, 1934, to relieve severe angina pectoris of 6 months duration. There was but little apparent improvement, and for the next 3 years the patient was unable to walk up a slight grade on account of chest pain. In view of a low basal metabolic rate ( $-32$  per cent) and some evidence of myxedema he took 1/10 gr. thyroid daily. For one year (1937-1938) he offered the information that his attacks were more marked after meals and dependent on the type of food ingested. After considerable experimenting with himself and with the lapse of time, he has been able finally to walk about 4 miles at a time without having an attack of angina pectoris, but he has learned to walk very slowly.

This patient's own comments on his well-being and freedom from attacks are interesting. Although the myxedema has had a quieting effect, he also has voluntarily slowed down, since his walking is methodical, never increasing the rate above 60 steps a minute. The evidence tends to show that a "slow pace in life" may allow a survival, at least in some cases.\*

\*In our case of coronary disease with severe angina pectoris treated successfully by total thyroidectomy in 1934, the interest is very much increased. A 47-year-old physician was treated by the same method without apparent benefit. After to total thyroidectomy he was completely relieved of his angina pectoris but he slowly developed myxedema. For this he took enough thyroid to hold his basal metabolic rate within normal limits. He felt well and despite adequate thyroid he has symptoms failed to suffer a recurrence of angina pectoris except when he pushed himself hard. He is still carrying on general practice at the age of seventy-three years. It is evident that he had a natural recovery of coronary sufficiency doubtless through the development of collateral circulation with a lowering of peripheral resistance—of a serious period of illness by the total thyroidectomy.

CASE 6. D.G., a 45-year-old jeweler was first seen medically in 1923. He had no complaint except that he had been rejected for life insurance on account of elevation of blood pressure, which was found to be 194/104. The patient was a dynamic person who enjoyed attending lodge meetings at least three or four times a week, and who took an active part in all the discussions. Although he was advised to "slow down," he refused to follow this advice, in view of the absence of symptoms.

The first attack of angina pectoris occurred in 1929, but in spite of this warning, the patient did not change his mode of living. Although he had no further attacks until 1934, the electrocardiographic tracings during the later years showed evidence of coronary-artery disease with myocardial involvement in the form of progressive changes in the T waves of Lead I. The attack in 1934 lasted 2 hours and required morphine for relief, but was not convincing enough to cause a change in the patient's habits. However, a second attack of coronary occlusion accompanied by paroxysmal auricular fibrillation in July, 1935, completely changed his idea of how to live and be happy.

Five years have elapsed since the severe attack of coronary occlusion, and during this period the patient has resorted to the use of nitroglycerin on the average of about once in 2 weeks, when he finds himself driving his automobile in difficult traffic (this is not a safe thing for him to do). The physical findings during this 5-year period have not changed. The blood pressure has remained around 200/110. Recently the vital capacity was 2400 cc., and there was no evidence of failure. Treatment has consisted of 5 gr. of quinidine sulfate twice daily, 1½ gr. of aminophylline three times daily, and 10 minims of Lugol's solution once daily.

Since the attack in 1935, the patient has adopted a strictly followed routine. He arises at 7 a.m., gets his own breakfast and walks about ½ mile to the bus very slowly (he says, "I have plenty of time and never rush for an oncoming bus, for there will be another right along"). Up to January, 1940, he took rest periods in the afternoon for about 45 minutes or 1 hour; since then he has felt so well that he has given them up. He works until 5:30 or 6:00. His meals are light, with dinner at 6:30. Although he retires at 7:30, he reads much of the night or until he is drowsy. Once or twice a week he spends an evening at either a lodge meeting or visiting friends, but at all times returns home not later than 10:30. He never goes out on Sunday. Although his production, per working hour, has decreased, he has been able to meet his financial obligations and has maintained a living income.

Here is another example of what careful living, in addition to a natural tendency to longevity, can do.

CASE 7. M.B., a 48-year-old schoolteacher, consulted us on June 12, 1926, because of the recent onset of tachycardia and dyspnea. On physical examination, she showed moderate cardiac enlargement, with a well-marked, rolling, mid-diastolic murmur at the apex, accentuation of the first apical sound and of the pulmonic second sound and an apical third sound. The heart rate at the apex was 160, at the wrist 104. The electrocardiogram showed auricular fibrillation with slight right-axis deviation. A high degree of mitral stenosis was clearly evident.

Digitalization was begun and maintained thereafter. For 14 years, the patient has continued to teach, with occasional short pauses caused by acute illnesses or to re-

cover from fatigue. Now, at the age of 62, she is ready to retire after a long, useful service. Despite increasing symptoms of pulmonary congestion and slight heart failure in the last 10 years, she has kept at work by the most careful regulation of her daily life. Her only activity has been to go to school, aside from brief vacation trips to the South in the winter or spring. She has rested during her long summer vacations. Often she has remained absolutely at rest after leaving school on Friday afternoon until she has gone again on Monday morning. She has survived several attacks of pulmonary infarction and of pneumonia and colds of lesser severity. For years she was able to drive her car but did very little walking. Only once or twice has she needed diuretic therapy, rest therapy and digitalis being adequate to prevent or control congestive failure.

When examined on June 15, 1940, the patient was in fairly good condition; she was convalescent from an illness of 7 weeks, probably precipitated by a small pulmonary embolism. She showed no evidence of heart failure. The heart rate was 56, and the rhythm irregular. The blood pressure was normal. The heart was large, with a loud systolic and a slight mid-diastolic murmur at the apex.

This case of rheumatic heart disease of more than average severity has permitted not only a considerable longevity but also a useful life of teaching through the carrying out of a sensible mode of life and the good fortune in being able to maintain a fair state of health and to avoid severe rheumatic infection. Familial longevity doubtless has entered into the picture.

#### DISCUSSION

Although this group of patients is small, it does represent a considerable number of cases of a similar character that physicians encounter during many years of experience. Often, however, the consultant may be unaware of the final outcome, nor does he always know what progress the patient has made subsequent to the consultation. It is important to recognize that the prognosis is as likely to be favorable as unfavorable in the majority of cases.

Three of the 7 cases reported showed serious heart trouble at the outset, with an unfavorable or even a grave prognosis; nevertheless, the patients experienced a natural or spontaneous recovery and did very well for a good many years. One of these patients was fortunate enough to have had an acute infection that saved him from a needless valvotomy, with a possibly fatal outcome.

In the second group were 4 patients, 3 of whom were able to continue to earn a livelihood for many years in spite of serious heart disease. This was accomplished undoubtedly by the careful program that each one mapped out for himself. The fourth patient, although he was unable to return to his original occupation, could without question employ himself in a less vigorous trade than that of a traveling salesman.

## SUMMARY

We have presented 7 cases of severe heart disease in which the patients, who at the onset of their illness appeared to have unfavorable prognoses, but through natural recovery or sensible living, were able to lead long and useful lives. This group emphasizes the statement that in acute heart disease "functional recovery may be so complete that the ultimate prognosis is good for many years

after." It is not to be inferred, however, that medical attention can be dispensed with. Furthermore, every person should seek medical counsel at the onset of symptoms, whether or not they are of cardiac origin.

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## THE TREATMENT OF HAND INJURIES\*

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THE basic surgical principles involved in the treatment of compound injuries are nowhere better exemplified than in the painstaking and purposeful treatment of injuries of the hand.

Treatment that ensures arrest of bleeding and protects the open wound from further contamination constitutes ideal first-aid care. Most cases require only the immediate application of a sterile dressing, held in place with the moderate pressure of a snug bandage and in severe cases reinforced with a light splint. The more promptly such a dressing can be applied, the less is the danger of contamination of the open wound with virulent organisms. With increasing experience, surgeons have come to realize that the most important potential sources of such organisms are the uncovered mouths and noses of excited and voluble bystanders, or of any persons who may be attempting to apply some form of emergency treatment without first masking their faces. In most cases of compound injury, uncovered hands, unmasked faces and instruments hastily sterilized by rinsing them in some antiseptic solution carry a greater menace for the patient than the instrument that caused the wound or the bacteria that may have been present on the patient's skin at the time of injury.

A second principle, sometimes forgotten until too late, is that diagnosis should always precede treatment. Every surgeon of experience knows how little information can be obtained by inspection or probing of an open wound. The hasty operator may forget that accurate and important information can be quickly obtained by examination of the function of the part below the site of injury. Division of the ulnar or median nerve,

for example, or of the flexor tendons of thumb and fingers can be recognized with certainty by simple tests that every first-year medical student knows full well and that too many residents and house officers have forgotten.

Once the extent of the injury has been determined, the next question is to decide what should be done immediately. Should cleansing of the wound be followed by operative repair of the injured structures, or should such repair be deferred until the question of wound infection can be answered with certainty? The time that has elapsed, the place where the injury was sustained, the first-aid treatment, the character of the injury itself and the facilities available for repair all come into consideration. Rarely would one attempt operative repair of an extensive wound if more than two hours had elapsed. Wounds sustained out of doors, in an automobile accident or in the street are likelier to be seriously contaminated than those sustained in a clean factory, a workroom or a kitchen. Careless or unthinking first-aid treatment may permit secondary wound contamination that leads to serious infection. Crushing injuries and deep and extensive lacerations are more difficult to transform into clean surgical wounds than clean cut incised wounds caused by glass or sharp metal. The attempt to repair a serious injury in an emergency or a ward dressing room without adequate assistance is almost certain to result in disaster. Difficult surgical procedures demand every advantage that a well-equipped operating room and expert assistants can provide.

Whether or not operative repair of injured tissues is to be undertaken immediately, every wound should be carefully and thoroughly cleansed at the earliest possible moment to convert the contaminated wound into a clean wound. To secure

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this result, I know of no more effective method than patient and thorough cleansing with ordinary white soap and sterile water, applied with soft sterile cotton and hands covered with sterile gloves, under eyes that are alert and mouth and nose that are completely masked (Fig. 1). Soap-and-water cleansing of at least ten minutes' duration is followed by thorough and prolonged irrigation of the open wound and all its recesses with warm physiologic saline solution. Charity may cover a multitude of sins, but the hope that

an open mind for the best method of meeting the problems in question. That there must be one most effective technic in treating open wounds in spite of the widely divergent methods and ideas in vogue whenever compound injuries are treated, no one would deny. Tomorrow may bring improved methods, but the immediate problem is to accomplish the best possible results with the facilities available today.

Briefly, then, the treatment of patients with hand injuries should include the following: gen-

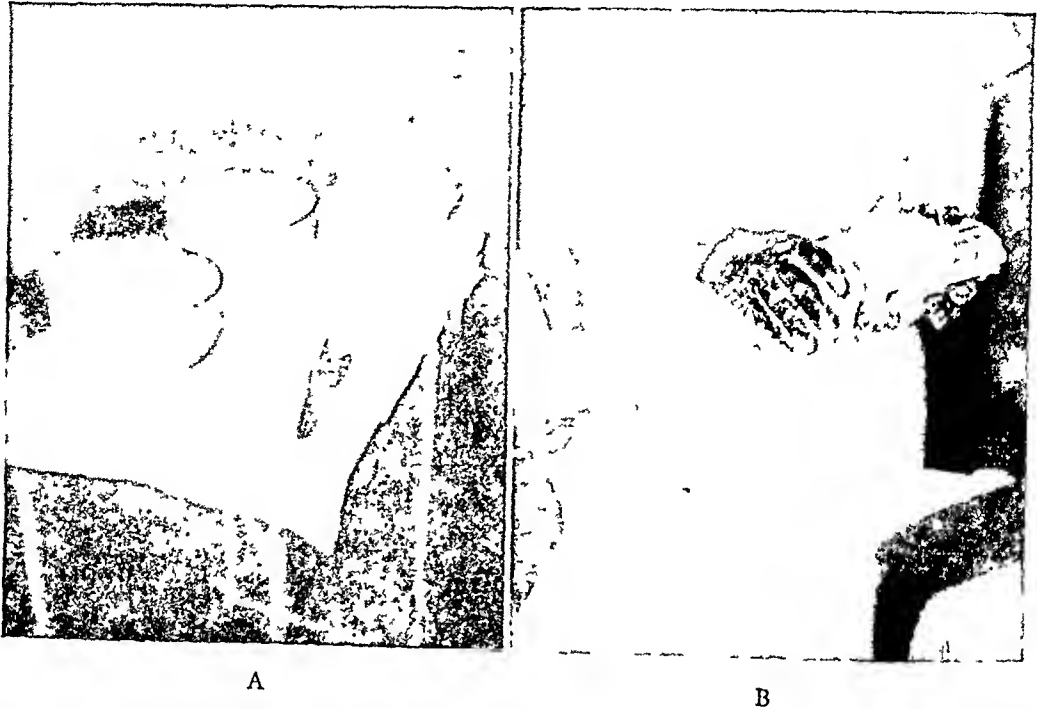


FIGURE 1. *Preparation of the Field of Operation.*

*A—a small table, with two basins of sterile water, a pile of soft cotton, a cake of plain white soap, a towel and dry sterile gloves, is ready beside the operating table. B—the cleansing of the field of operation is gentle, but thorough and painstaking, and is continued for at least ten minutes (Koch<sup>1</sup>, reproduced by permission of the publisher).*

sulfanilamide crystals can cover a multitude of virulent organisms, which may have come from the open mouth or uncovered nose of well-intentioned persons giving first aid, and completely neutralize their harmful effect is certain to result in disappointment. The value of chemotherapy should not be minimized, but the relative importance of the ounce of prevention and the pound of cure is just as great in wounds of the hand as in any potential disaster.

Time and space do not permit the discussion of many details that are essential in actual surgical treatment, or of the basis on which conclusions that may seem too dogmatic are founded. Nevertheless these conclusions are based on a considerable experience and a constant search with

eral anesthesia in cases of severe injury; a bloodless field secured with the aid of a blood-pressure cuff inflated to 250 mm. of mercury; incisions that permit adequate exposure of injured tissues, retracted muscles and tendons and that do not cut across flexion creases (Fig. 2); gentle handling of tissues, no matter how much greater the expenditure of time; accurate hemostasis; the use of silk ligatures and sutures of the finest caliber that afford the required tensile strength; reduction of fractured bones without interposition of foreign material; repair of divided tendons by a method that leaves the tendon ends as free as possible from the irritating action of foreign material; suture of divided nerves with the finest possible silk suture that includes in its

bite only the epineurium (Fig. 3); and, finally, complete and accurate wound closure without drainage. These details of treatment are carried

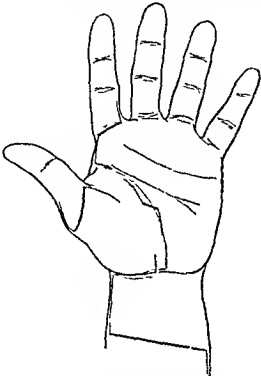


FIGURE 2. Lines of Incision.

Incisions for securing adequate exposure should be made to be parallel with flexion creases and not across them. Median incisions of the fingers and forearm and cruciate incisions should always be avoided (Koch<sup>1</sup>; reproduced by permission of the publisher).

out not in blind adherence to a routine inherited from the past, but as the result of a serious effort to learn by experiment, by observation of one's

Perhaps no one of these details is likelier to arouse controversy than the suggestion to close the wound accurately and without drainage; yet it is just as vital to secure healing by primary union for the patient who has sustained a division of nerves and tendons as it is for the patient whose hernia has been repaired or whose stomach has been anastomosed to the small bowel. It is even

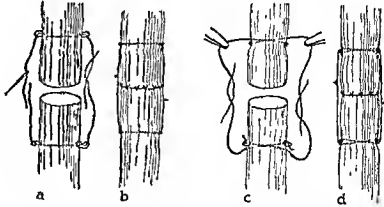


FIGURE 3. Technic of Tendon Suture (Mason).

Both methods (a and b, and c and d) are consistent with the important criterion that the free ends of the two segments be as free as possible from foreign material. Experimental studies indicate that in the second method (c and d) there is less tendency for the tension suture to cut through the tendon and permit partial separation of the sutured ends (Koch<sup>1</sup>; reproduced by permission of the publisher).

more important, since any wound infection, no matter how trivial, impairs the usefulness of structures, such as tendons and joints, the function of



FIGURE 4. Crushing Injury of the Hand Treated by Immediate Soap-and-Water Cleansing, Wound Repair and Immediate Covering of the Extensive Raw Surfaces with Grafts of Intermediate Thickness (patient of Dr. Michael Mason).

Appearance of the hand before operation.

own results and those of others and by thoughtful consideration of what methods afford the best possibility of securing the desired result of healing with a minimum loss of time and function.

which depends on complete freedom of movement. I should even say that if the wound cannot be closed accurately and without tension because of loss or destruction of covering tissue, it

is the obligation of the surgeon to provide covering tissue by the use of a flap or graft, so that

demand immediate attention, but to miss the most favorable opportunity to secure closure of a wound

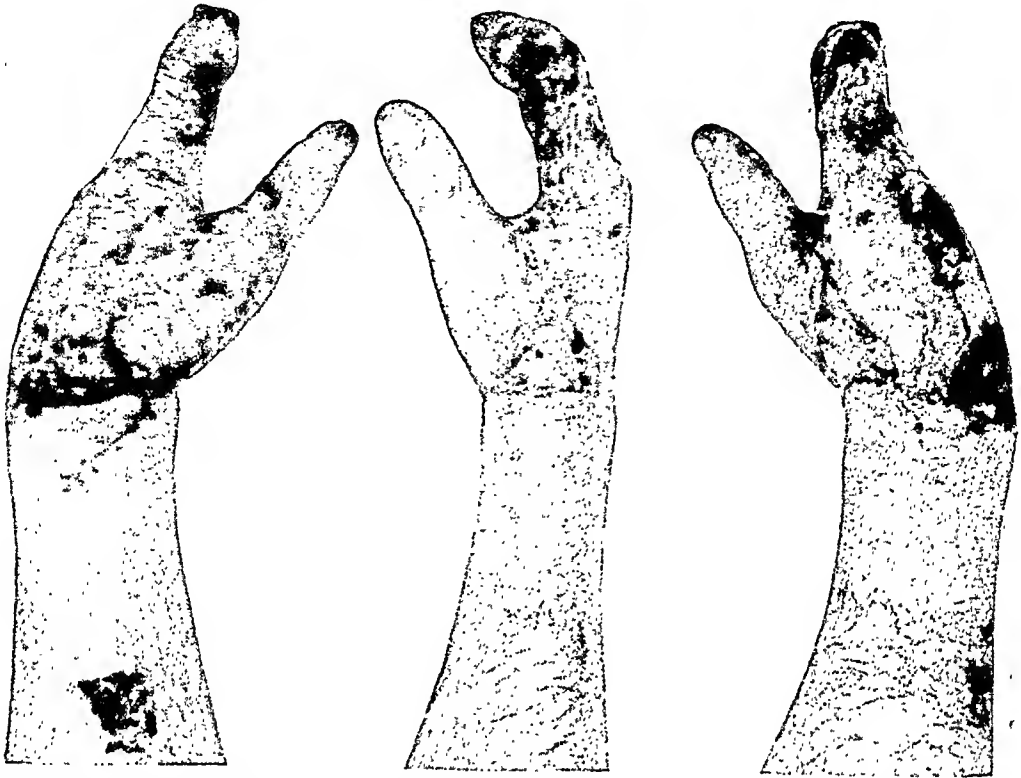


FIGURE 5. *Crushing Injury of the Hand Treated by Immediate Soap-and-Water Cleansing, Wound Repair and Immediate Covering of the Extensive Raw Surfaces with Grafts of Intermediate Thickness (patient of Dr. Michael Mason). Appearance of hand at the primary dressing.*

the desired result of immediate wound closure can be attained (Figs. 4, 5 and 6). If the use of a

with the aid of a graft or a flap where there has been extensive loss of covering tissue and to await

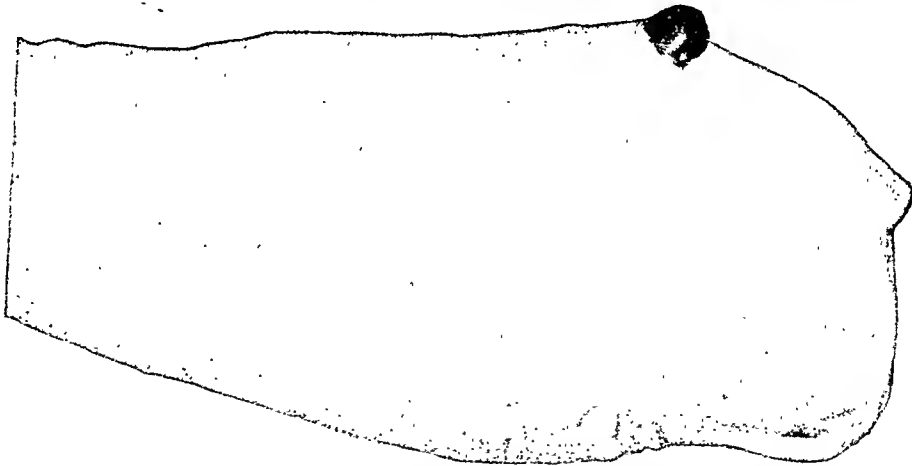


FIGURE 6. *Crushing Injury of the Hand Treated by Immediate Soap-and-Water Cleansing, Wound Repair and Immediate Covering of the Extensive Raw Surfaces with Grafts of Intermediate Thickness (patient of Dr. Michael Mason).*

*Hand immobilized with aluminum splint and enveloped in a large gauze dressing, bandaged under moderate pressure, and left undisturbed for fourteen days after operation.*

flap or graft is necessary, one rarely undertakes repair of divided nerves or tendons until wound healing is complete. The latter procedures do not

the formation of granulation tissue and the crippling fibrosis invariably associated with it before attempting to secure wound closure are misfor-

tunes for both the surgeon and the patient

When the wound has been closed, whether by suture or graft, a large pressure dressing consisting of fluffed gauze, cotton waste or sea sponges is applied over the entire wound area, and the part immobilized with the aid of a light aluminum splint. Inflamed and injured tissues need rest, and the rest secured by the compression bandage and splint is uninterrupted, if possible, until the time when the sutures should be removed. If the treatment has been painstaking and well performed, one may wisely leave the dressing and wound untouched. The patient is watched carefully for evidence of impaired circulation and wound infection; the dressing is left undisturbed.

Finally, one cannot refrain from emphasizing

the oft-repeated precept. The outcome of any case depends primarily on the surgeon who first sees the patient. If his treatment is skillful and well considered, rarely will anything more need to be done at a later date, and if further treatment is necessary the conditions will usually be favorable. If the treatment rendered immediately after the injury is haphazard and thoughtless, it too often happens that no surgical care, no matter how skillful or painstaking, can compensate for the initial neglect of the basic principles of treatment of compound injuries.

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## MEDICAL PROGRESS

### KIDNEY DISEASE

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SINCE my last review,<sup>1</sup> the varying problems of Bright's disease have continued to be attacked in many ways: by clinicians who have attempted to observe patients at the bedside more accurately than heretofore; by laboratory workers who have devised ingenious experiments to produce, prevent or cure experimental nephritis, and even by surgeons who have tackled the lesions of nephritis by surgery rather than by more orthodox medical methods. Hence any reader in this general field of medical literature soon has his appetite surfeited. To avoid mental indigestion, he is driven, perforce, to include in his diet only those literary delicacies that seem most digestible for his particular type of mind. This year, therefore, I have made no attempt to summarize all the communications of the last twelve months but instead have selected for discussion a group of papers that I have found both readable and stimulating.

One of the ideas that nowadays attract almost every clinician is the thought of being able to use plasma in some form for purposes of blood transfusion. The possibility of utilizing concentrated plasma protein solutions in the management of renal edema associated with reversed albumin globulin ratios and lowered blood protein concentrations springs naturally to mind. Thus the ob-

servations of Aldrich and Boyle<sup>2</sup> are important as being among the earliest on record in this particular effort. These workers used concentrated solutions of serum protein as a diuretic in a group of patients with nephrosis. They dehydrated pooled serum to make its normal protein concentration four times normal, and injected the resultant solution by vein in doses that varied from 25 to 65 cc. In most of their cases, diuresis followed such treatment and continued until the edema was eliminated. The possibilities of developing this method of therapy in certain types of renal edema are promising. Concentrated plasma, in fact, may prove to be an excellent diuretic not only in renal edema but also in other conditions in which water retention depends on disturbed physicochemical relations in the blood and tissues.

A few years ago a charming doctor from Dublin named O'Shaughnessy visited this country. He spoke in New England at several of our local medical meetings—a fiery, enthusiastic young Irishman, sincerely interested in the possible value of omentopexy for the treatment of angina pectoris. His idea was to bring a piece of omentum through the diaphragm, attach it to the heart apex and thereby stimulate the formation of a new blood supply to the myocardium. His work did not stir up great excitement in Boston, but everyone who heard O'Shaughnessy speak was impressed by his sincerity and uprightness. The announcement of

All articles in this series will be published in book form the current volume is *Medical Progress Annual 1940* (Springfield Illinois: Charles C. Thomas Company 1941) \$4.00.

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his death on active service with the British Expeditionary Force in Flanders made all his American friends feel badly, for no one could meet him without hoping to see him again. But at least his ideas carry on. MacNider and Donnelly,<sup>3</sup> modifying his method, have attempted to establish in animals an adventitious circulation in the kidney by omentorenopexy, and Weeks, Steiner, Mansfield and Victor<sup>4</sup> appear to have successfully treated experimental renal hypertension by the operation of splenorenopexy. By the last procedure, it seems, collateral circulation between the splenic sinusoids and the capillaries about the renal tubules was provided, with an improved circulation through the kidneys and a resultant fall in blood pressure. When the fused spleen and kidney was later removed, the blood pressure soon returned to its previous level of hypertension. Perhaps eventually we shall hear more of the clinical usefulness of O'Shaughnessy's ideas and of their application in directions other than he supposed.

Goldblatt's work continues to inspire clinicians to hunt carefully for patients with hypertension whose abnormal blood pressure level is caused by unilateral renal conditions. A variety of new cases have been reported: perhaps the most peculiar one is that described by Koons and Ruch,<sup>5</sup> which concerns a seven-year-old child with a Wilms's tumor complicated by hypertension. The tumor did not appear to be the source of the hypertension since, when an exploratory operation was performed, extensive metastases were seen and felt, and these presumably would have perpetuated hypertension after nephrectomy if the tumor had manufactured any pressor substance. Yet actually the hypertension disappeared when the kidney and the primary tumor were taken out. Koons and Ruch explain this happening on the assumption that, since the tumor practically surrounded the kidney, it caused renal ischemia and acted in much the same way as the cellophane membrane that Page and his associates<sup>6</sup> placed around the kidney in animals to produce experimental hypertension. If this explanation is correct, this is the first clinical confirmation on record that Nature has a means of duplicating in man so bizarre a renal lesion as the one made synthetically by Page in the laboratory.

Many typical cases of unilateral atrophic pyelonephritis cured temporarily, at least, of hypertension by nephrectomy are now on record, so that an increasingly large group of such patients are being followed for lengthening periods. A patient of mine,<sup>7</sup> whose case was reported in 1940, continues to have normal blood pressure; to the list have been added during the past year a Cana-

dian case reported by Patch, Rhea and Codnere<sup>8</sup> and 5 new cases reported by Barker and Walters,<sup>9</sup> of the Mayo Clinic. Everyone seeing these cases maintains a proper attitude of conservatism over end results. Palmer, Chute, Crone and Castleman<sup>10</sup> express the generally accepted viewpoint: for success in this operative approach to hypertension, only those cases must be selected for surgery in which there is no recurring pyelitis or other abnormality on the apparently normal side.

Neurosurgeons have become a little less vociferous than they have been in previous years. To be sure, Peet, Woods and Braden,<sup>11</sup> staunch proponents of such complicated operations as bilateral supradiaphragmatic splanchnectomy with lower dorsal sympathetic ganglionectomy, have reported results in 350 cases. They claim that in slightly over half the cases in their series there was significant reduction in blood pressure and that after operation, clinically speaking, their patients' disability was improved in the vast majority of cases. This is a good record, which speaks for itself. On the other hand, Davis and Barker,<sup>12</sup> of the thiocyanate school, claim that bilateral splanchnic section fails to give relief to patients who cannot obtain equal benefit from the proper use of this drug. They still maintain that many patients with hypertension respond favorably to thiocyanate and that the drug is not unduly dangerous, and apparently, they continue to use it with satisfaction. The perfect treatment of hypertension is still undiscovered.

When the American College of Physicians met in Boston this spring, no single paper was read that provoked more discussion in the corridors, bedrooms and dining rooms of the Hotel Statler than that of Page and his associates<sup>6</sup> on the use of kidney extract in the treatment of experimental and clinical hypertension. Beforehand, everyone wondered how Page would describe his most recent work, and afterward, how convincing were the results reported.

Page has elaborated a theory that is interesting. He believes that the diseased kidney may produce a substance which raises blood pressure and that this, in turn, can be neutralized and rendered inert by an antistubstance developed in the normal kidney. With this thought in mind, he at first carried out experiments on animals in which extracts from normal kidneys were used in an attempt to counteract experimentally produced hypertension. Elevated blood pressure was induced by several different means and appeared controllable by properly graduated doses of normal renal extracts. These results were sufficiently convincing to Page to make him try the next

hurdle At the meeting of the College of Physicians, he reported on 19 human cases of hypertension treated in similar fashion He drew no conclusions that were at all unguarded However, he produced evidence to suggest that the prenteral injection of renal extract in his cases appeared, on the whole, to have been of some value in treatment In certain cases, for example, there was marked improvement in the condition of the eye grounds, in the cardiac symptoms and in the blood pressure levels On the other hand, severe reactions occasionally developed, owing, he believes, to the protein content of the extracts employed He concluded his remarks, wisely and sanely, by stating that the use of kidney extracts in the treatment of certain cases of hypertension probably has some merit and at least deserves further study Knowledge concerning the true usefulness of the technic or even of the idea behind it is too fragmentary to bear much discussion Yet no one who heard Page speak could fail to believe that his work deserves watching

When one leaves the laboratory and turns more closely to the bedside for the basis of his reading, he encounters several worthwhile papers Lupus erythematosus is much in the public eye at the moment Hence the paper by Suckney and Keith<sup>12</sup> is interesting They studied the kidneys in 15 fatal cases and concluded that there is no distinct renal lesion peculiar to the disorder In 8 of their cases, the kidneys appeared normal, in 2, glomerulonephritis was found, and in 5, there was no more specific form of nephritis than a certain amount of proliferation of the glomerular endothelium, together with irregularity and thickening of its basement membrane Thus lupus erythematosus cannot be regarded as having any typical form of kidney lesion attached to its pleomorphic pathology

The relation of tonsillar infection to nephritis has been discussed perennially for a long time Illingworth,<sup>14</sup> in England, is the latest clinician to claim that tonsillectomy neither cures nephritis nor prevents its progress, in fact he even goes so far as to suspect that tonsillectomy may predispose to nephritis or may actually precipitate an attack The paper was printed a year and a half ago, and his ideas seem not to have been repudiated or generally supported by his British colleagues

Acute nephritis and the acute exacerbations that so often occur in the course of chronic nephritis have also received due consideration Hayman and Martin,<sup>15</sup> in an excellent paper, have analyzed the histories of 22 cases of acute nephritis The

most interesting point in their paper is that about two thirds of their patients recovered completely. Acute nephritis, too, as they point out, is, on the whole, a disease of young people and, contrary to Illingworth's views, is likely to be precipitated by acute upper respiratory tract infections involving the throat, sinuses and ears

That acute glomerulonephritis may follow so simple a skin infection as impetigo is emphasized in a paper by Fletcher<sup>16</sup> He picked out of the Johns Hopkins Hospital Clinic 11 cases in which glomerulonephritis followed impetigo or some other superficial skin infection, although, to be sure, beta hemolytic streptococci were not infrequently found in these cases on throat as well as on skin culture That skin infections may be followed by so serious a complication as glomerulonephritis in certain cases is worth remembering

Seegal, Lytle, Loeb, Jost and Davis<sup>17</sup> have re-emphasized the relapsing character of chronic nephritis They say that the life history of a patient with chronic nephritis is often punctuated by repeated attacks of acute nephritis superimposed on the basic underlying chronic lesion Such attacks are usually accompanied by transient decreases in renal function or by sudden marked hematuria One of their patients with chronic nephritis had, they believe, several attacks of acute nephritis in the course of a few years This paper is an interesting attempt to establish the complete picture of chronic nephritis through utilization of the method of careful follow up studies on a small group of patients observed over a long period To my mind their ideas carry considerable weight It is highly probable that repeated acute insults, each with or without complete healing, do much to account for the characteristically slow progress of many cases of chronic Bright's disease

Now that the ordinary clinician is becoming educated to recognize gout more readily than he used to, gouty nephritis is again receiving attention Talbot and his co-workers<sup>18</sup> at the Massachusetts General Hospital have written a clever paper to remind us of what our English forbears knew so well that most subjects with gout show some evidence of renal damage Certainly they have performed some painstaking and superb studies on earmarking the characteristic renal lesion of gout—clinical studies that would have amazed old worthies like William Cadogan or Benjamin Franklin, who thought they understood the gouty diathesis The urates seemingly can be filtered through the gouty kidney but are reabsorbed with difficulty Drugs like cinchophen and Salycan depress further urate resorption but stimulate urate clearance, colchicine, stringently

enough, has no particular effect one way or the other, so that at present why it appears to behave so beneficially in gout is uncertain.

The sulfonamides are so popular that naturally they have been used abundantly in the treatment of various urinary infections. Cook<sup>19</sup> has written a helpful paper describing which ones of the new members of the family are of particular help in combating genitourinary infections caused by a variety of different organisms. It is obvious that the causative agent must be established and that each case is best treated individually. In Cook's experience, sulfanilamide, dimethyldisulfanilamide and sulfanilylsulfanilamide were most effective against gram-negative bacilli, beta-hemolytic streptococci and the proteus bacillus, whereas sulfapyridine seemed more useful to combat staphylococcal infections. Sulfathiazole proved useful against gram-negative bacilli and staphylococci but was not very efficacious against beta-hemolytic streptococci. Finally, when the renal function was poor, azosulfamide seemed to be the drug of choice since it appeared to have little or no injurious effects on the kidney. In this connection it is worth remembering that all members of this family, even when properly used, may bother the renal system. The sulfonamides tend to precipitate in the collecting tubules or even in the ureters and bladder unless due care is taken, and thus they act as renal irritants. I like Arnett's<sup>20</sup> rule in using these drugs—a minimal intake of 3000 cc. of fluid each day, with an output of 1500 cc. or more, and careful watching of the urine for the presence of hematuria. No patient enjoys having to put up with urologic manipulation to rid himself of the chemical calculi that may form when he uses these medicines.

\* \* \*

On the whole, the past year has been one of activity in the advancement of knowledge regard-

ing Bright's disease and its treatment. The trend of the times is to pay increasing attention to renal physiology, so that a great deal of work is now going on with pressor substances and their relation to hypertension. On the other hand, clinicians still continue to see cases of chronic nephritis frequently and to hope for the development of more secure methods for the cure and prevention of this disease than now exist.

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CASE RECORDS OF THE  
MASSACHUSETTS GENERAL HOSPITALANTE MORTEM AND POST MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

## CASE 27291

## PRESENTATION OF CASE

A seventy-two-year-old man entered the hospital for study.

The patient was seen for the first time by a staff member of this hospital nine years before admission, when diagnoses were made of irritable heart,—possibly on the basis of coronary disease,—auricular fibrillation and myxedema. Shortly afterward, he was confined to bed for twelve weeks, suffering from what was either pulmonary infarction or an incidental pulmonary infection. Seven years before admission, he had an attack of dyspnea, which lasted fifteen minutes and was not accompanied by pain, palpitation or cough. He remained in bed for three days, after which he returned to his usual activities. Apart from occasional shortness of breath, he remained well for the next seven years, and during the summer preceding his admission he played golf without untoward effect. Four months before entry, the patient suffered a violent nosebleed, and a month later noticed the onset of gradually increasing dyspnea, even while walking on level ground. A severe attack of dyspnea developed during a walk ten days before admission; it lasted ten minutes and, again, was not accompanied by other symptoms.

The patient had been constipated for some time and had noticed an urgency and frequency of urination, with the passage of small amounts, and a nocturia of three times a night. Several days before entry, a dry cough had developed.

When thirty-two years old, the patient had suffered from mumps complicated by severe bilateral orchitis. Shortly after this episode, he noted marked loss in sexual power, which proceeded to complete impotency. His skin became fine in texture, his beard regressed, the pubic and axillary hair fell out, and his phallus decreased in size. There was no marked loss of strength or of weight. He did not experience hot flashes at any time. It was thought by some that the pitch of his voice became higher.

He had four children, who were living and well.

On physical examination, the patient's features were definitely eunuchoid in appearance; it also

had somewhat the appearance of that seen in myxedema. The skin as a whole was of fine texture, the speech was slow, and the hair of the head was normal but that of the extremities, axillas, pubic region and perianal region was absent; the testes were small, no prostate tissue could be felt.

The neck veins were moderately distended, with visible pulsations. The left border of the heart was 3 cm. outside the mid clavicular line,—the heart was appreciably larger than it had been nine years previously,—and a soft systolic murmur was heard at the apex and to the left of the sternum. The aortic second sound was greater than the pulmonic. The rhythm was irregular, the blood pressure 160 systolic, 90 diastolic. A few rales were present at the right lung base. The abdomen was normal. There was a minimal pitting edema of the shins.

The temperature was 98°F, the pulse 88, and the respirations 20.

The urine showed a + test for albumin. The blood showed a red cell count of 4,520,000 with a hemoglobin of 13.4 gm (photoelectric-cell technique), and a white cell count of 8400. The blood sugar was 82 mg and the cholesterol 101 mg per 100 cc. The 17-ketosteroid excretion in the urine was very low, but not absent, on two occasions, the actual figures were 1.4 and 1.2 mg per twenty-four hours. There was no excess of follicle stimulating hormone in the urine, the basal metabolic rate was -15 per cent.

An x-ray film of the chest showed the diaphragm to be high on the right side and its respiratory movements limited. There was mottled dullness along the right border of the heart, and in the angle between the heart and diaphragm; the costophrenic sinus on the right side was shallow. The heart shadow was considerably enlarged in its transverse diameter, and there was a definite bulge of the right auricle. The supracardiac shadow was not increased, the appearance of the aorta was not remarkable, and there was no visible calcification or mediastinal masses. X-ray examination of the skull showed the sella turcica to be rather large and bridged, but no abnormalities of shape or erosion of the clinoid processes could be seen. The pineal gland was visible and in the usual position. The bones of the skull were unusually heavy. There was no evidence of increased intracranial pressure, and the usual blood-vessel markings were present.

The electrocardiogram showed an unusual ectopic auricular rhythm, regular at 160 or more; this was considered to represent an ectopic auricular tachycardia. For the most part, there was a



2:1 ventricular response, with an occasional ectopic ventricular contraction. The ventricular rate was 85;  $T_1$  was low,  $T_2$  slightly inverted,  $T_3$  inverted.  $Q_3$ , which varied from 2 to 3 mm. in length, was inverted,  $R_4$  upright, and  $T_4$  low.

The patient was given digitalis; the heart slowed but remained irregular, with a varying degree of auriculoventricular heart block. The edema had cleared on the fourth hospital day. Ten days after admission, the patient was started on testosterone propionate, 12.5 mg. intramuscularly three times weekly. This therapy was continued until three days before death. At two weeks, a chest plate showed that the process in the lungs had cleared; the diaphragm was in the usual position, and the lung fields were clear; the heart shadow was roughly triangular and was increased somewhat in size, the increase being largely to the right.

The patient was discharged under the care of his physician.

He made a follow-up visit two months after discharge. At that time, everything seemed to be going very well. He felt considerably stronger; he had noted a return of sexual power.

At 4:00 in the morning after the follow-up visit, the patient's wife was awakened by nightmarish noises from her husband. She failed to arouse him and finally called his physician, who arrived at 5:30 a.m. The patient was in moderately profound coma, with Cheyne-Stokes breathing and pinpoint pupils, but without obvious paralysis. The blood pressure was 200 systolic, 90 diastolic, and the pulse was 60. Three hours later, his condition was essentially unchanged, so that aminophyllin was administered, with the result that breathing improved and the patient roused to the point of movement and answered a few simple questions, although his words were scarcely intelligible. That evening, another administration of aminophyllin wrought no change; there was urinary incontinence, respiration had improved, the pulse was irregular at 80, the blood pressure was 185 systolic, 90 diastolic, and the pupils were constricted.

The following day, the patient was still semiconscious and incontinent, with Cheyne-Stokes breathing, a blood pressure of 150 systolic, 75 diastolic, and a pulse of 60. That evening, coma deepened, the temperature was  $102^{\circ}\text{F.}$ , the pulse was faster, and the patient seemed choked up.

The next day, the temperature was  $104^{\circ}\text{F.}$ , the respirations 50, and the pulse 100. Coma was even more profound, and diminished breath sounds and rales were heard throughout the right chest. The patient died that day.

## DIFFERENTIAL DIAGNOSIS

DR. EDWIN B. ASTWOOD:\* We have, in brief, a seventy-two-year-old man who, at the age of thirty-two, had a severe orchitis as a complication of mumps, followed by complete sexual impotency and certain other endocrine changes, but who remained well until nine years before entry, when he began to have symptoms referable to his heart. He finally entered the hospital for study, presumably because of increasing dyspnea and signs at that time of moderate cardiac decompensation. This cleared on digitalis and rest, and he was discharged well. He died suddenly, or at least died very shortly after a sudden attack, apparently of something entirely different. I do not believe that one single disease can explain everything. We might briefly discuss the three aspects that are most outstanding.

In the first place, the cardiac condition was longstanding, nine or ten years, and was accompanied by cardiac enlargement and finally by symptoms of failure, with the presenting symptom of dyspnea. I do not consider the mention of myxedema sufficient to account for the enlargement of the heart, or definite enough to account for the cardiac condition. The presence of dilatation of the right auricle, taken together with the ectopic auricular tachycardia, might indicate that there was myocardial damage in the right auricle. Auriculoventricular block also suggests myocardial damage, and in a man of seventy-two the most probable diagnosis is a coronary arteriosclerosis, with possibly myocardial infarction. I do not believe that the electrocardiograms are contradictory to such a diagnosis. When the patient entered the hospital, the physical signs were in keeping with an increased venous pressure, with pulmonary congestion and perhaps with pleural fluid and enlargement of the liver. This condition cleared on rest and digitalis, and probably represented a mild cardiac decompensation.

The cause of death, however, seems to have been a second type of condition. If the first assumption—that the patient had coronary arteriosclerosis—is correct, it is reasonable to assume that he had arteriosclerosis elsewhere, although no mention is made of it. He did have hypertension, and sudden coma coming on in a hypertensive man of seventy-two is suggestive of a cerebrovascular accident. The absence of localizing signs and paralysis indicates not a corticostriatal lesion, but perhaps a thalamic or mid-line lesion. A lesion in the pons might be more probable because of the pinpoint pupils and final hyper-

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pyrexia. Whether the condition was thrombosis, embolus or hemorrhage rests on more details of the actual events leading up to the accident. This patient with complete impotency for forty years had a sudden restoration of sexual activity, and encountered an eventually fatal corn; this, I think, strongly suggests cerebral hemorrhage, possibly in the pons.

The third point to be considered is the nature of the endocrine disturbance. We are told in the history that the patient had mumps complicated by bilateral orchitis, and that this was the cause of loss of sexual power and loss of hair. There are several points that might be against such a concept. In the first place, it is very rare indeed for this type of orchitis to produce complete destruction of the testicular tissue. Experimentally, 2 per cent of viable testis tissue is sufficient to allow fairly normal endocrine function of the testis. Furthermore, complete azoospermia following such an orchitis is extremely rare, and still rarer would be complete destruction of the interstitial elements. Another thing against the possibility that the testicular atrophy was due to this cause is that the patient had complete impotency, which is scarcely credible even on the basis of complete castration. The loss of all body hair is something one does not usually associate with loss of testicular function. These three points are better explained by pituitary insufficiency, because all are symptoms of Simmonds's disease. This is not complete hypophyseal deficiency, however, because the patient maintained his weight and noted no loss in strength. There are a few other things that would support the concept of pituitary damage. The low metabolic rate, -15 per cent, and the myxedematous appearance, without real myxedema—the skin was soft and smooth, and the cholesterol value was 101 mg per 100 cc.—one would associate not with myxedema but with hypothyroidism of hypophyseal origin. The low 17 ketosteroids, as Dr. Albright has shown, could mean that he was an old and debilitated man suffering from some nonspecific illness associated with an absence or a great reduction of adrenocortical function and an absence of testicular function. All this endocrine disturbance may indicate a man of seventy-two who had no testis function, and the other endocrine changes may have been the result of old age. However, I should think that the major endocrine disturbance was hypopituitarism, and although I have never heard of such a sequela, the change apparently occurred at the time when he had mumps; it is possible that it might have been a complication of mumps, just like other glandular complications, or was perhaps related to meningitis.

In summary, I should consider the cardiac condition as coronary sclerosis, with infarction, the terminal event, cerebral hemorrhage, perhaps pontine, and the endocrine disturbance, hypopituitarism.

Dr J. H. MEANS: I saw this patient in consultation, and the question that was put up to me was as follows: "This patient has had myxedema for some time and appears to have a combination of myxedematous heart and coronary disease, with arrhythmia. Will you please see him and advise concerning treatment for hypothyroidism?" Because of his heart disease, they thought that they ought to go cautiously with thyroid. I saw him and did not think he had myxedema. I was impressed more than anything else with the factor of eunuchoidism. The man was emphatic in saying that this dated from the mumps. I was not certain whether anyone could get complete destruction of the testes from such an orchitis. I raised that, however, as one possible explanation, but also, like Dr. Astwood, suggested that it could be, and more probably was, on the basis of hypopituitarism.

One point about the diagnosis of myxedema: if this patient had had ordinary myxedema nine years before entry, and had not had treatment with thyroid in the interim, it would be impossible to have a picture of this sort. He would have been in an advanced stage of classic myxedema by the time of admission. The longest we have known any patient with myxedema to go is fifteen years—that is the utmost life expectancy. But after nine years with no appreciable change, we can say that he certainly did not have any ordinary myxedema.

One other point that should be brought up is whether the therapy in any way contributed to his demise. I suggested that it might benefit him, but I now believe that this may have been bad advice.

Dr FULLER ALBRIGHT: I went through the same reasoning as Dr. Astwood did and came to the same conclusion. I should emphasize one other bit of evidence, which Dr. Astwood did not make use of: there was no excess of follicle-stimulating hormone in the urine. If the patient had had complete destruction of his gonads by mumps and if there was no pituitary disease, he should have had a positive follicle-stimulating hormone test. The fact that it was negative is strong evidence that the pituitary gland was the origin of the disturbance.

The question has been raised about the rationale of administering testosterone in this case. It is our belief that testosterone has a much wider effect on the patient than merely to stimulate sec-

ondary sex characteristics. I refer especially to its effect on nitrogen metabolism, which consists in a marked sparing of protein. Unless there are some definite contraindications, I am inclined to believe that patients with lack of testosterone production should receive this hormone. Furthermore, we have found in patients with panhypopituitarism—that is, underfunction of all parts of the anterior portion of the pituitary gland—that testosterone has a markedly beneficial effect.

The question has also been raised whether testosterone therapy in any way led to the patient's death. One must probably proceed with caution in administering testosterone to elderly patients for fear that the increased libido might lead to excesses, which might be bad for their cardiovascular system. In this particular case, no such increase in libido resulted, and I think we can dismiss this possibility. Furthermore, the symptoms at the time of death do not convince me that the primary cause of death was coronary thrombosis.

One other possibility occurs to me. Patients with panhypopituitarism have a marked tendency to hypoglycemia. Testosterone therapy, by inhibiting the conversion of proteins into sugars, might easily increase this tendency. I should at least raise the question whether the beginning of the acute symptoms that led to his death was not hypoglycemia. The semicomatose condition in which he remained for two days is most suggestive of this condition.

#### CLINICAL DIAGNOSES

Coronary heart disease.  
Auricular tachycardia and fibrillation.  
Hypogonadism.

#### DR. ASTWOOD'S DIAGNOSES

Coronary sclerosis, with infarction.  
Cerebral hemorrhage, probably pontine.  
Hypopituitarism.

#### ANATOMICAL DIAGNOSES

Coronary sclerosis, with fresh thrombosis, left descending branch.  
Adenoma of the pituitary, neutrophilic type.  
Hypopituitarism.  
Atrophy of the thyroid gland.  
Atrophy of the testes.  
Chronic fibrous orchitis.  
Hypertrophy of the heart.  
Eunuchoidism.

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: The post-mortem examination showed obvious heart disease. The

heart weighed 560 gm. The patient had severe coronary sclerosis, and there was fresh thrombosis of the left descending branch, which had not as yet led to any gross infarction. On anatomic grounds, this was the only possible cause of death discovered, because in the brain there was no hemorrhage or evidence of thrombosis or cerebral softening. Of course, I cannot rule out hypoglycemia, and Dr. Albright makes out a strong case for it. The testes were a little small, evidently fibrosed. On microscopic examination, the left one appeared absolutely fibrotic. In our sections, we could not find a tubule or any sign of spermatogenesis. The right testicle was only three quarters destroyed; there were some persistent tubules and some mitotic figures among the spermatogonia. There was some effort at sperm formation, but it was incomplete and no sperm was present. I could not find any unmistakable interstitial cells in either testis. So that I think there is no doubt that there was extensive testicular destruction by mumps but, as one would expect, not complete destruction, and there must have been another reason for the marked depression in function of the remaining testicular tissue. The adrenal glands seemed a little small and the cortices possibly narrow, but histologically I could not see anything definitely abnormal. The thyroid gland was distinctly atrophied and weighed only 10 gm. Microscopically, the acini were small, and there was considerable increase in fibrous tissue. The pituitary gland was largely replaced by a neutrophilic, presumably nonfunctioning adenoma. Only a small rim of anterior lobe tissue persisted on one margin. It seems fairly evident that pituitary function was depressed because of compression by the tumor.

#### CASE 27292

#### PRESENTATION OF CASE

A fifty-seven-year-old housewife entered the hospital complaining of pain in her leg.

The patient had been known to have hypertension for about four years, with systolic blood-pressure readings reaching as high as 230. She felt well, however, until four hours before admission, when a smothering sensation developed under the upper sternum, without dyspnea, pain or cough. She lay down, and half an hour later a gradually increasing pain and tingling appeared in her left leg and was soon followed by numbness, cold and paralysis of this extremity. There was also transient tingling in the right foot. Her physician gave her morphine subcutaneously.

The patient had complained of frequent head-

aches and slight dyspnea on exertion for the previous month. There was no history of rheumatic fever, chills, night sweats, anginal pain or substernal oppression.

The patient's mother had died of "shock", one sister had hypertension.

On examination, the patient was pale and appeared anxious and acutely ill. The heart was enlarged to the left, with systolic and diastolic murmurs at the base, heard best over the aortic area. One examiner believed there might have been a mitral systolic murmur. The rhythm was regular. The blood pressure was 160 systolic, 110 diastolic. Occasional moist rales were heard throughout the chest. The abdomen was normal. The patient was unable to move her left leg, which was cold and a mottled pink below a definite line drawn horizontally through the lower margin of the vulva. In this leg no pulsations of the femoral, popliteal, posterior tibial and dorsalis pedis arteries were palpable, and the sphygmomanometer did not oscillate below the mid thigh or in the calf. Pulsations were present throughout the right leg.

The temperature was 99°F, the pulse 100, and the respirations 28.

An electrocardiogram showed normal P waves and QRS complexes in all four leads. The T waves were upright, but of low amplitude, the ST segments were very slightly depressed.

Two and a half hours after admission, the patient could move her left ankle, but not the toes. The leg was warmer, pulsations were palpable in the femoral artery to a point just below the profunda femoris branch, and the sphygmomanometer oscillated at the mid-thigh and calf, but not at the ankle.

Three hours after admission, an incision was made along the left femoral artery below Poupard's ligament under local anesthesia. Death occurred nine hours after admission.

#### DIFFERENTIAL DIAGNOSIS

DR CLAUDE E. WELCH: This is a short story, and it might be just as well to list first the few diagnoses that might be considered. These are peripheral embolus, a coronary attack, with marked spasm in the extremity, and a dissecting aneurysm of the aorta. Several points are of considerable importance in making the diagnosis. Of course, it is quite obvious as one reads the history that the clinical diagnosis was an embolus in the left leg.

I shall consider some features not consistent with that diagnosis. In the first place, the patient had had a hypertension for many years, but

four hours before admission a smothering sensation in the chest developed. This is a very important symptom, it seems to me, because the patient remembered it well enough to tell about it. It could have been due either to dissecting aneurysm or to coronary thrombosis. It is of interest that we recently had under treatment a man with acute coronary thrombosis whose initial symptom was pain in the leg. This pain was so severe that it was not until several hours later, after he had been given morphine, that he recognized that he had pain in the chest. The pain in the leg turned out to be due to spasm, and it was later proved that he had an acute coronary thrombosis. A smothering sensation is not at all typical of embolus.

There is nothing in the past history of any interest.

Clinical examination of the heart would mean something to Dr. Blard, but it does not mean much to me. The electrocardiograms are of some interest because the T waves were upright. All I know about electrocardiograms is that with coronary disease the T waves are often inverted. This electrocardiogram therefore offers a little evidence against coronary disease. At the onset the findings in the leg were typical of occlusion at the level of the bifurcation of the iliac artery. Apparently, the patient's pulsations returned, in part, while she was on the ward. That would lead the surgeon to believe that the embolus had descended to a spot where it might be accessible.

Apparently operation was performed; at least the patient was explored for an embolus and died nine hours after admission.

If the symptoms had been due to embolus, there was no reason to expect death at this time. Patients die usually of an unrelated cause,—coronary thrombosis or gangrene,—days or even weeks later, so that death at that time is not consistent with the single diagnosis of embolus. It seems to me, therefore, that many features in this case are inconsistent with the diagnosis of embolus, some are inconsistent with coronary thrombosis. There is nothing inconsistent with the diagnosis of dissecting aneurysm of the aorta, and that is the one that I make.

DR WILLIAM RICHARDSON: I should like to mention just one thing. I certainly agree with Dr. Welch, but I wonder if this is going to turn out to be the type of dissecting aneurysm that is due to media necrosis cystica, or whether syphilis may not actually have been present in this case.

I should like to ask Dr. Welch about spasm in connection with coronary disease. Is there a complete loss of pulsation?

DR. WELCH: In the case I mentioned, the patient had previously recognized vascular disease in the leg. There were no pulsations before or after the attack of coronary disease. We had another patient with absent pulsations immediately after an attack of coronary thrombosis; they returned after the acute phase had subsided.

DR. WILLIAM B. BREED: It seems obvious that the people who had charge of this patient did not think she had a dissecting aneurysm. They operated on the leg on the basis that she had an embolus. I am surprised that she did not have more pain in the chest, in the back and in the abdomen. Also, the fact that this happened rather suddenly makes me think that perhaps she did not have a dissecting aneurysm. I should favor an embolus, which was the diagnosis that the person who was in charge of her made.

DR. EDWARD F. BLAND: Is Dr. Welch disturbed by the diagnosis of dissecting aneurysm and by the finding of such good pulsations in the right leg in contrast with complete absence at first in the left, followed later by the appearance of pulsations in the upper portion of the affected leg? Do you often see that situation in dissecting aneurysm?

DR. WELCH: The peripheral circulation after dissecting aneurysms that go far down the aorta is very confusing. I am sure I have seen them follow a course like this in one or two cases. One has to assume a certain amount of spasm of the large vessels to account for the changing symptoms.

DR. BREED: The patient might perfectly well have died of a pulmonary embolus from the right side of the heart.

DR. BENJAMIN CASTLEMAN: That is very rare.

DR. BREED: Pulmonary emboli associated with coronary disease or occlusion are not at all uncommon.

DR. CASTLEMAN: The source of the emboli is very rarely from a mural thrombus overlying a right ventricular infarct. They may arise from an auricular thrombus associated with fibrillation or from the peripheral veins in the legs.

DR. RICHARDSON: I think the patient died of dissecting aneurysm, probably of pericardial tamponade.

DR. WELCH: Would it be amiss to ask Dr. Bland to interpret the cardiac situation for us?

DR. BLAND: The electrocardiogram is all right from the description. The diastolic murmur as described means aortic regurgitation. We do not know about the blood serologic findings, of course. An aortic diastolic murmur appears after dissection in a number of cases, probably because of

distortion of the aortic valve ring, owing to dissection backward toward the heart. If this murmur had not been present before and had appeared after the episode, it would be strong evidence in favor of dissection of the aorta.

DR. BREED: On the other hand, the electrocardiogram was taken only two hours after the onset of the disease, and you certainly could not rule out coronary disease or occlusion by an electrocardiogram taken at that time, could you?

DR. BLAND: No.

DR. CASTLEMAN: The surgeon is not here, but I shall read his operative note:

A careful re-examination of the extremity was made just before operation, to be sure that the signs were not improving as they had previously. The level of demarcation was the same,—just below the knee,—the foot was cold, the popliteal pulse was still absent, and the femoral pulsation was the same as previously.

A 10-cm. longitudinal incision was made under novocain, extending from Poupart's ligament downward over the course of the femoral artery. The artery was found to be pulsating throughout the entire extent of the exposure, which was for 4 cm. below the origin of the profunda femoris. The profunda itself was also pulsating, although all pulsations were definitely diminished. There was apparently some inflammatory reaction around the artery, since the femoral vein was quite adherent to it. The vein was dissected off and divided, and it was found that the upper end of the vein bled profusely, showing that there was no thrombosis in it.

Attention was then turned to the artery. After some deliberation, and in view of the definite clinical findings, it was decided to open the artery; this was done longitudinally through a 1-cm. incision, 4 cm. above the profunda. A free flow was obtained from above, moderately free flow from below. No thromboses or emboli were seen or extractable. The artery was then closed.

#### CLINICAL DIAGNOSES

Embolus to left femoral artery.

Hypertensive heart disease.

#### DR. WELCH'S DIAGNOSIS

Dissecting aneurysm of aorta.

#### ANATOMICAL DIAGNOSIS

Dissecting aneurysm of aorta.

#### PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At autopsy, we found an enlarged heart, weighing 700 gm. The coronary arteries showed a moderate degree of sclerosis but no evidence of occlusion. In the ascending aorta, several centimeters above the valve, was a T-shaped intimal tear in the intima, which communicated with a dissecting aneurysm. The ex-

ternal perforation had occurred just below this region into the pericardium, which was full of fresh blood. The dissection had continued down the aorta into the left external iliac and femoral arteries, to a point about 5 cm below Poupart's ligament, at which point the lumen was occluded by the opposing intimal surfaces. The incision at operation was a few centimeters below the point of occlusion. Had the surgeon known that this was a dissecting aneurysm at the time of operation, he might have attempted the operation described by Gurin,\* that is, the making of a nick in the occluding intima above, to allow the blood from the dissecting channel to come down and enter the original stream. This might have relieved the pressure in the aneurysm and perhaps prevented external rupture. In Gurin's case, the circulation of the leg was restored, but the patient died six days later.

There is one other thing that occurred in this case that is quite unusual. The external perforation through the adventitia must have been relatively slow, because the blood had extended from the adventitia of the aorta into the adventitia of the main pulmonary artery and its branches into both lungs, appearing as subpleural hemorrhagic extravasations in the interlobar septa. At present, we have not finished studying the microscopic sections, but we are quite certain that the etiology of the dissection was media necrosis aortica cystica. There were no atheromatous plaques or areas of arteriosclerosis in the ascending aorta at the site of the tear. There was no evidence of syphilis or of an inflammatory reaction that would go with syphilis. I might say, Dr Richardson, that syphilis

rarely, if ever, produces dissecting aneurysm.

DR RICHARDSON: My reasoning was false. I did not realize that a diastolic murmur could occur as a result of a dissecting aneurysm. If I had known this, I should not have mentioned syphilis.

DR BLAND: Was there any abnormality of the aortic valve, other than the deformity of the aortic ring, to account for the diastolic murmur?

DR CASTLEMAN: No.

DR BLAND: Dr. Chester S. Keefer once suggested that such a murmur might be due to the reflux of blood through the rent in the aorta, a possibility that seems to me most unlikely. I do not believe there is that much reflux of blood with diastole, unless possibly at a much later date when a double aorta has developed in the few who survive. The first explanation seems more reasonable. In perhaps a fourth of the cases, an aortic diastolic murmur appears immediately after the dissection.

Does syphilis of the aorta protect against this condition?

DR CASTLEMAN: I do not know. It is quite possible that the medial scars that are formed in syphilis might be a protection against it. We have never seen dissecting aneurysms of the aorta produced by syphilis.

DR BREED: May I ask again about the pain in dissecting aneurysm? Do you think the pain in this case was less? I am not trying to defend my diagnosis. I am asking for information.

DR BLAND: I should say that at least 90 per cent of patients have severe pain. Double barreled aortas are occasionally found post mortem, with no history of an acute illness corresponding to the dissection.

\*Gurin D, Bulmer J W and Derby R. Dissecting aneurysm: diagnosis and operative relief of acute arterial obstruction due to this cause. *New York State J Med* 35:1200-1202, 1935.

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## POPULARIZATION OF ADVANCES IN MEDICINE

THE June 14 issue of *Science News Letter*, a weekly publication devoted to popularized accounts of advances in the sciences, makes the following startling introductory statement concerning papers presented at the Cleveland meeting of the American Medical Association: "*Six new successful treatments, promising relief or cure for the suffering of thousands of men and women, were reported. . . . Hundred per cent control of gonorrhea is made possible by sulfa drug. Crude liver extract is the new remedy for gout and arthritis. Salts of gold are being tried secretly on human rheumatism patients. Sex hormone treatment gives new hope for those with cancer of prostate gland. Iodized oil helps sinus disease, and x-rays are advised for Hodgkin's disease.*" As one reads the subsequent paragraphs, one is told that the drug,

sulfathiazole, has been responsible for 100 per cent cures of gonorrhea in three days; that the use of crude liver extract in the treatment of patients with gout and arthritis was promptly followed by a disappearance of symptoms, particularly in the former disease; that a gold compound, calcium aurothiomalate, has been successfully used in the treatment of experimentally produced arthritis in mice; that female sex hormones or castration inhibits the growth of cancer of the prostate; that the injections of iodized oil into the sinuses result in the subjective improvement of patients suffering from sinusitis; and that patients with Hodgkin's disease are relieved by x-ray or radium treatment.

In commenting on these abstracts, the medically trained writer could reasonably state that sulfathiazole is a standard accepted remedy for gonorrhea, although no one has ever before obtained 100 per cent effectiveness, a claim that requires careful follow-up studies over a period of months or years; that in judging the value of any new treatment for gout,—the present treatment is reasonably satisfactory,—the possibility of spontaneous remissions of the disease must be excluded; that experimentally produced arthritis in mice is undoubtedly a different disease from human arthritis, the cause of which is unknown; that the efficacy of the use of female sex hormones in the treatment of cancer of the prostate has been discussed, pro and con, for several years; that subjective improvement in patients with sinusitis is a poor yardstick for measuring the value of any therapeutic agent; and that x-rays and radium have been used for the treatment of patients with Hodgkin's disease for several decades. In other words, three of these "new, successful treatments" have been previously reported, two require confirmation of their value, and for one no claim for efficacy in human beings has been made. Undoubtedly many, if not all, of these points were brought out by the speakers at the meeting, and it is unfortunate that popularized reports in periodicals and newspapers are, in many instances, so garbled.

The public should, of course, be informed concerning advances in medicine, since lay education

of this sort is one, if not the most effective, means of promoting the health of the nation. However, such reports, particularly those in regard to widespread diseases such as gonorrhea, arthritis and sinusitis, should be accurate and conservative; if "successful remedies" are announced year after year, the layman will become suspicious, and lay support of the medical profession—a matter of vital importance at the moment—will be weakened.

### MEDICAL EXPLORERS

Nor a few physicians who have traveled extensively have returned home to write of their explorations and thus to give pleasure and instruction to their fellow colleagues and many others. Some have set out on scientific missions, such as Mungo Park, the young Scottish surgeon, whose *Travels in the Interior Districts of Africa* (1799) may still be read as a thrilling account of individual adventure. Other famous doctors described their travels for pleasure. Two may be mentioned: Richard Bright's *Travels from Vienna through Lower Hungary* (1818), an account of a post-graduate tour, illustrated with Bright's original drawings, and Thomas Hodgkin's *Narrative of a Journey to Morocco* (1866), the story of a trip with his patient, Sir Moses Montefiore. To these two groups must be added a third, composed of those describing a vacation tour or a particular service with the Army or Navy. In this category would fall the well-known book by Oliver Wendell Holmes, *Our Hundred Days in Europe* (1887), and the fine account by the late Harvey Cushing entitled *From a Surgeon's Journal* (1936).

The whole group of travel books by doctors extends into several thousand volumes. There have already been gathered in one library four or five hundred volumes, and many more are known. Doctors in general have added greatly to the knowledge of the world, and their reminiscences have been of much interest to their fellow colleagues. Few, however, have engaged in much more than the ordinary types of travel. Mungo Park would be considered an explorer of the first class, as would the American, Elisha Kent Kane, who visited the Arctic.

At the present time there must be added to these individuals the name of Richard Upjohn Light, who in the last ten years has made two unusual trips by aeroplane, accounts of which have been published. The first one was a privately printed book, *Journal of a Seaplane Cruise Around the World, August 20, 1934, to January 24, 1935* (1937). On this trip, Light, with Robert French Wilson as his radio operator, circumvented the globe by aeroplane, except for the trip across the Pacific from Manila to Vancouver. Thus he became the first American to fly from continental United States eastward to the Philippine Islands. His log of the journey was accompanied by his carefully drawn maps of the country over which he passed. He made many notes of particular medical interest, and one of his reports, after his visit to Labrador, was separately published in the October 25, 1934, issue of the *Journal*. In addition there are many notes in the book about medical conditions in Greenland and accounts of his visits to various hospitals in Europe. This journey, taken seven years ago, was a pioneer effort in exploration by aeroplane and was widely recognized by geographers as a trip of unusual importance. Following this exploration, Light was made a member of the American Geographical Society and later was elected a councilor of that distinguished scientific body.

Under the auspices of the American Geographical Society, Light has now published his account of another aeroplane trip, this time over Africa. A review of the extraordinary book appears in this issue of the *Journal*. His account is a fitting climax to an unusual career in the air, which began in 1930. Light flew over Central America in 1932; later he photographed parts of the Rocky Mountains from Vera Cruz in Mexico northward to Salt Lake City. His trip around the world in 1934-1935 has already been mentioned. In 1937-1938, prior to the trip across Africa, Light and his wife flew westward across North America, southward through Mexico and Central America, then eastward across South America to Rio de Janeiro. During this decade, Light has become the outstanding physician of his time in the world of aerial exploration.



## MEDICAL EPONYM

### HUTCHINSONIAN TEETH

On May 18, 1858, Jonathan Hutchinson (1828-1913) presented "Report on the Effects of Infantile Syphilis in Marring the Development of the Teeth" before the Pathological Society of London. This paper appears in the *Transactions of the Pathological Society of London* (9: 449-455, 1858).

For a considerable time past, I have been in the habit of recognising in a certain very peculiar development of the permanent teeth an indication that their possessor had in infancy suffered from hereditary syphilis. . . . I will now pass to the conclusions arrived at.

. . . . *There is a peculiar condition of the teeth, which results from the influence of hereditary syphilis, and . . . the most frequent features of this condition are the following:*—*a. Smallness.*—The teeth stand apart with interspaces, and are rounded and peggy in form instead of flat. *b. Notching.*—They usually exhibit in their border a broad shallow notch, or at times, two or three (serrated). Owing to their softness, these teeth rapidly wear away, and this notching is thus often obliterated, but when markedly present, it is one of the most decisive conditions. *d. Colour.*—Instead of the clear, smooth, white exterior of good teeth, they present a dirty greyish surface, totally destitute of polish and rarely smooth. No amount of cleaning will materially alter this feature which owes its existence, I believe to the great deficiency of enamel. *e. Wearing down.* As before observed their softness from deficiency of enamel renders them liable to premature wearing down. . . . *f. The signs mentioned apply almost exclusively to the incisors and canines and in fact the grinders are usually altered in a very much less degree. Their surfaces are often more uneven than those of healthy teeth, and now and then they present tubercular projections of a very peculiar character. . . . The above remarks apply only to the permanent set.*

R. W. B.

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

#### SUDDEN DEATH OF UNKNOWN CAUSE DURING THE SIXTH MONTH OF PREGNANCY

A twenty-seven-year-old para II had had no prenatal care. Physical examination during her first pregnancy, two years previously, was negative; the blood pressure and the heart and lungs were normal. There was no history of operation. The first pregnancy had terminated normally at term with a living child. The physician

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, Secretary, 330 Dartmouth Street, Boston.

who had attended the patient previously was informed of the present pregnancy very casually when making a visit at the house because the child had measles. He made no examination. A very short time after this, the patient complained of a severe pain and died before a physician arrived.

*Comment.* Since it is known that emboli during pregnancy cause death, it seems likely that such a condition was the cause of sudden death in this case. There was no history of heart disease. The patient had had a baby two years earlier, at which time the attendant physician said that her heart was normal. She had had no infections since then, so that it is fair to infer that there was no cardiac lesion. The blood pressure was said to have been normal with her first pregnancy, and consequently hypertension as a cause of cerebral hemorrhage can be ruled out. Furthermore, had she had a cerebral hemorrhage, it is unlikely that she would have died so quickly. It is said that she had a pain and died. It is not stated where the pain was localized. The uterus may rupture spontaneously at five or six months, but death occurring so quickly after the rupture is unlikely, and there was no history of vaginal bleeding.

It is unfortunate that the medical examiner did not insist that an autopsy be performed.

#### DEATHS

DOUGHERTY—HARRY L. DOUGHERTY, M.D., of Jamaica Plain, died June 1. He was in his forty-third year.

Born in Nickelsville, Virginia, he attended William and Mary College and received his degree from the University of Louisville School of Medicine in 1925. He served his internship at the United States Marine Hospital in Chelsea and then opened offices in Jamaica Plain. He was a member of the staff of the Faulkner Hospital.

Dr. Dougherty was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, his parents, two daughters, two sons, three brothers and four sisters survive him.

NORTON—GEORGE P. NORTON, M.D., of Fitchburg, died June 12. He was in his sixty-eighth year.

Dr. Norton received his degree from the Bellevue Hospital Medical College, New York City, in 1895. He was former city physician and district medical examiner and had been on the staff of the Burbank Hospital for twenty-nine years. At the time of his death, he was chief medical examiner for the draft board under the Selective Service Act.

A former president of the Worcester North District Medical Society, he was also a member of the American Medical Association.

His widow, two sons, a daughter and a grandchild survive him.

TRACY—JOHN M. TRACY, M.D., of Springfield, died July 9. He was in his seventy-fourth year.

Born in Saugerties, New York, he attended St. Mary's College, New York City, and received his degree from George Washington University School of Medicine in 1898.

Dr. Tracy began practice in Springfield in 1899, where he was a former member of the School Committee and a member of the staff of the Mercy Hospital and the city health department. At the time of his death, he was a lieutenant colonel in the United States Army Medical Reserve.

He was a fellow of the Massachusetts Medical Society and the American Medical Association.

Two sons and a daughter survive him.

## MISCELLANY

### GASTRIC LAVAGE IN ADULTS

Failure to find tubercle bacilli in the sputum even after repeated examination of successive specimens, is no justification for ruling out the possibility of tuberculosis. The least certain of the methods commonly used is the staining of the direct smear of the untreated sputum. One supplementary method is to examine the stomach washings for tubercle bacilli especially in children, who are likely to swallow the sputum. Roper and Ordway (*Gastric Lavage in Adults with Pulmonary Tuberculosis*, *Am. Rev. Tuberc.*, 43:543-556, 1941) advocate its wider use for adults and offer impressive evidence of its value. Abstracts of their article follow.

The examination of fasting gastric contents by smears for tubercle bacilli, first reported in 1898, proved unreliable, and the need for culture and animal inoculation was demonstrated. Since 1927, numerous articles have been published regarding this procedure in juvenile tuberculous patients. More recently the test has been used on adults.

This report presents the findings obtained by guinea pig inoculations of fasting gastric contents of tuberculous and nontuberculous patients. By the addition of this procedure to the usual methods, recovery of tubercle bacilli in tuberculous patients was practically doubled.

The studies were carried out at the Metropolitan Life Insurance Company Tuberculosis Sanatorium during a three-year period in which approximately 1000 patients were admitted of whom 135 were diagnosed as having active pulmonary tuberculosis and the remainder were considered to be nontuberculous. This afforded opportunity for using controls.

Since 1929, the percentage of minimal cases admitted has almost trebled, in patients with moderately advanced disease it has decreased slightly, and in those with far advanced involvement it has declined to one-third the former figure. Yet the percentage of positive sputum cases has fallen despite the more frequent use of animal inoculation (from 45.2 per cent in the period 1926 to 1928 to 34.8 per cent in the period May, 1936 to May, 1939).

Of the 135 tuberculous patients of the present study, 34.8 per cent gave positive recovery by sputum examinations alone. The addition of gastric lavage almost doubled this percentage, namely, 63 per cent.

Sharp distinction is made between sputum and fasting stomach contents. Sputum refers to the bronchial secretion that is actually expectorated by coughing or clearing the throat. The gastric specimen contains the bronchial secretion which has gained entrance into the pharynx and has subsequently been swallowed. Gas-

tric lavage was initially employed in children because of their inability to expectorate. By means of this same test in adults, many positive results are obtained among those whose efforts to raise sputum are unsuccessful, as well as in many of those producing unsatisfactory or negative sputum.

Sputum produced by the tuberculous patient may contain tubercle bacilli on one day and none on the next. The same variability occurs with gastric washings. Stelm recommends that the test be given on each of three successive mornings.

The test is of assistance not only in the diagnosis but also in the management of the tuberculous patient. After years of treatment the sputum may disappear or become negative, whereas the gastric contents may still exhibit virulent tubercle bacilli.

The procedure of obtaining the gastric specimen causes only slight discomfort to most persons and is not harmful on the other hand repeated forceful voluntary efforts to expectorate are uncomfortable and may be harmful. The value of proving or disproving the clinical and roentgenologic diagnosis of pulmonary tuberculosis is obvious and of equal significance is the conclusive demonstration of the subsequent disappearance of tubercle bacilli from the bronchial secretions of tuberculous patients under treatment. Knowledge of these facts is of sufficient import to justify the use of gastric lavage whenever it is indicated by the absence or negativity of sputum.—Reprinted from *Tuberculosis Abstracts*, July, 1941.

## CORRESPONDENCE

### THE CLOSED STAFF HOSPITAL

To the Editor: An editorial in the June 5 issue of the *Journal* pointed out many of the advantages of the closed staff hospital but failed to mention any of the unsalutary practices that sometimes exist.

That any member of the medical profession who is technically equipped, adequately trained, ethical and desirous of keeping constantly up to date in his profession will have no difficulty in obtaining permission to practice in his local hospital is not always true. Members of medical boards who are responsible for nominations to the staff are not always actuated by purely altruistic motives. Prejudice, jealousy and ambition to increase their practice regardless of the Golden Rule may influence their decisions. Moreover, members of these committees are often self-perpetuating either by reason of their position as chiefs of services or because of their appointment by lay boards who govern the hospital. Nominations to the staff therefore are not always based on the considered judgment of the doctors' peers, since they are made by physicians who may not be responsible to or representative of the staff. As a result, members of medical boards may prohibit a physician from using the hospital for an indefinite time without just cause, thus interfering with his livelihood, preventing his professional development and results in inferior service to his patients.

The correction of these unfair practices is definitely the business of organized medicine such as the Massachusetts Medical Society. If physicians who serve on executive or advisory committees in hospitals could be elected by ballot by the entire staff for limited terms (possibly one to three years), it would not only reduce these discriminatory practices but also contribute to the democratic administration of hospitals as a whole. Such recommendation by the Massachusetts Medical Society would no doubt be received by hospital trustees or directors with

the same spirit of co-operation as were similar constructive suggestions by other reputable medical organizations, such as the American Medical Association and the American College of Surgeons.

CARL BEARSE, M.D.

483 Beacon Street  
Boston

## BOOK REVIEWS

*Focus on Africa.* By Richard Upjohn Light, M.D. Foreword by Isaiah Bowman, Ph.D., LL.D. 4°, cloth, 228 pp., with 323 illustrations and 14 maps. New York: American Geographical Society, 1941. \$5.00.

In the winter of 1937-1938, Dr. Richard Light, an explorer of note, who has traveled extensively in his airplane, and also a neurosurgeon, now in practice in Kalamazoo, Michigan, who was trained by Dr. Harvey Cushing, flew across Africa from Capetown to Cairo. His wife, who is also an expert in aviation, acted as co-pilot, radio-man and photographer. This extraordinary trip is now described in a narrative augmented by a series of superb photographs of the country over which he flew. Dr. Light writes in a delightful and informative style, and the book will make delightful reading for physicians interested in the broader aspects of medicine and travel.

Although there is not much strictly medical material in Dr. Light's account, nevertheless he gives sidelights on the people of South Africa and some of the problems connected with the immense industries of gold and diamond mining. In addition to the unusual photographs giving a new idea of the terrain of a country as viewed from the air, the book is illustrated by numerous maps carefully depicting the course of his flight. It may well be said, as noted by Dr. Isaiah Bowman, who writes a foreword to the book, that Dr. Light has put details "against their parent backgrounds, effects against their causes" in an admirable and graceful manner. He is indeed one of the leaders of modern exploration whose standard is "To broaden those earth-bound glimpses. . . ."

*Lipidoses: Diseases of the cellular lipid metabolism.* By Siegfried J. Thannhauser, M.D., Ph.D. Edited by Henry A. Christian, M.D., LL.D., Sc.D. (Hon.), F.R.C.P. (Hon., Can.). (Reprinted from *Oxford Loose-Leaf Medicine*.) 8°, cloth, 370 pp., with 78 illustrations. New York: Oxford University Press, 1940. \$6.00.

Harvey Cushing once remarked that the field of general surgery at first appealed to him as being most worth while to master; before long he realized that surgery of the central nervous system was less well understood and therefore was more appealing. This quickly proved to be too broad an area for his temperament, and hence surgery of the brain became of paramount importance. But the brain was too large so that next its center, the pituitary gland, attracted his main attention; finally the secrets of the anterior lobe of this small body proved sufficiently elusive to satisfy his medical inquisitiveness. This is a good story of how zeal to make important discoveries in a small corner of medicine is often developed.

The author of this book evidently feels about medical research as Cushing did. For he began as a competently trained teacher and investigator of general medicine; his imagination became stimulated by how little was known of the general subject of the lipids, and this book is the crystallization of twenty years of painstaking, critical study of the matter.

The Oxford University Press always publishes stylishly. Hence the format of the volume is excellent. The type is easy and agreeable to read, the illustrations on the whole are clear, and the job of indexing is well done. The plan of the work, too, is easily comprehensible: first a discussion of the physiology and chemistry of lipid metabolism; next a chapter on hyperlipemia; then chapters on the xanthomatoses, primary, secondary or localized; and finally two concluding chapters on those confusing diseases known familiarly to the well read as Gaucher's disease and Niemann-Pick's disease. A scholarly bibliography of some eight hundred references is neatly dovetailed in between each chapter. The net result is a fine monograph that will serve for the next several years as the standard work of reference about unique disorders caused by disturbances in the metabolism of fat.

*Photodynamic Action and Diseases Caused by Light.* By Harold F. Blum, Ph.D. 8°, cloth, 309 pp., with 25 tables and 50 illustrations. New York: Reinhold Publishing Corporation, 1941. \$6.00.

This book justifies the two distinct purposes that prompted the American Chemical Society to sponsor a series of scientific and technologic monographs on chemical subjects. First, it closely connects the fields of physics, chemistry and medicine in the study of photodynamic action and diseases caused by light. Secondly, it presents a thorough historical survey of the progress already made, and points out directions in which research should be extended.

This study is vastly important at a time when industry is introducing many new chemicals, especially dyes, in our defense program. Their possible toxicity in relation to light has been recently described. This deleterious combination has been recognized for almost the past five decades, but has been neglected by most physicians. The author's attempts to correct or clear many incorrect or vague statements in the literature are worth while. Many diseases have been ascribed without proof to the action of sunlight. Other diseases are readily recognized in certain endemic areas, but are missed in other places because of ignorance of their existence. Few physicians recognize this sensitivity to light among human beings. Today, with the widespread use of ultraviolet radiation and the increase in the use of photodynamic substances for diagnostic purposes and in chemotherapy, physicians should be alert and cognizant of their possible effects when the patient is subjected to sunlight, to radiation from mercury-vapor lamps and carbon-arc lamps and to roentgen rays, for great damage can be done. Dermatologists have been more or less aware of the untoward results that occur after the unfortunate use of these substances without knowledge of them. This has been demonstrated in the use of dyes and ultraviolet radiation in the treatment of psoriasis, and their use in cosmetics and industrial chemistry.

The book is divided into four parts: the introduction describes the nature of radiation and its general biologic effects; the second part presents the general photochemical aspects of photodynamic action; the third section describes the diseases caused by light in domestic animals; and the fourth part describes the diseases produced by light in man. Each phase is adequately treated, and each part can be read independently.

It is a book that can be found useful by all students, and it should be in the library of all physicians and veterinarians.

# The New England Journal of Medicine

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## THE ARNOLD-CHIARI MALFORMATION\*

### Diagnosis, Demonstration by Intraspinal Lipiodol and Successful Surgical Treatment

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BOSTON

TWO patients who at operation were found to have a malformation of the cerebellum were recently admitted to the Neurological Service at the Massachusetts General Hospital. The rarity of the syndrome, the discovery of the importance of intraspinal lipiodol as a diagnostic method,

since they worked separately, both have been credited with making the first observation. Later, Gredig and Schwalbe<sup>3</sup> published a scholarly account of the embryology and anatomy of this anomaly, and Russell and Donald<sup>4</sup> and Penfield and Coburn<sup>5</sup> have recently discussed the pathologic physiology.

The chief characteristics of the anomaly as given by these different writers are:

It is primarily a congenital malformation of the medulla oblongata and the cerebellum, both of which are herniated through the foramen magnum into the cervical spinal canal (Fig. 1). The part of the cerebellum that is herniated is the inferior portion of both hemispheres, improperly called the "tonsils."

This herniation secondarily leads to the following disturbances: obstruction to cerebrospinal fluid circulation resulting in hydrocephalus—the cerebrospinal fluid passes from the ventricles into the spinal canal and cannot re-enter the cranial vault, where it is normally absorbed, because of the mass of tissue obstructing the foramen magnum; stretching and injury of the lower cranial nerves; pressure on the spinal cord and the medulla oblongata; and deformity of the cerebellum.

An associated meningocele, together with the Arnold-Chiari malformation, causes most of the patients to die in infancy.

The basal meninges, particularly the pia and arachnoid, are greatly thickened.

Even though this is a rather clear-cut pathologic entity, the Arnold-Chiari malformation is usually discovered at necropsy, not having been suspected during life.

In the last few years, Parker and McConnell<sup>6,7</sup> and Aring<sup>8</sup> have reported a group of patients

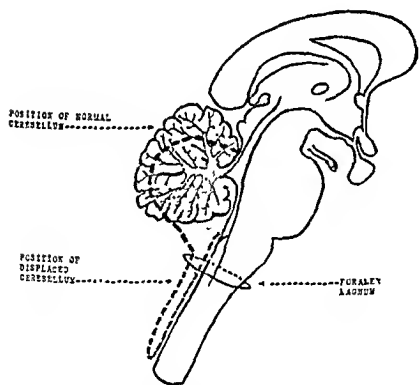


FIGURE 1. Diagram of Brain Stem and Cerebellum in Sagittal Section.

and the need of emergency surgery in the treatment of these cases have prompted us to present them in detail.

Arnold,<sup>1</sup> in 1894, and Chiari,<sup>2</sup> in 1895, published original descriptions of this malformation, and

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who during adolescence and early adulthood presented a symptom complex suggestive of a posterior-fossa or high-cervical tumor, but who at operation were found to have the same deformity of the medulla oblongata and cerebellum that Arnold and Chiari had described. These patients did not have a meningocele or other congenital anomalies, and several survived after suboccipital and high-cervical decompression. There was marked thickening of the basal leptomeninges. Whether the deformity of the cerebellum in these cases is also a congenital anomaly is less certain.

The first of our patients is representative of the type of case described by Parker and McConnell; the second illustrates the type described by Arnold and Chiari. We are using the term "Arnold-Chiari syndrome" to designate the aggregate of symptoms and signs by which this malformation manifests itself.

### CASE REPORTS

CASE 1. J.P. (No. 89142), a 17-year-old schoolboy, was admitted to the Neurological Service of the Massachusetts General Hospital with the following symptoms: suboccipital discomfort, periodic nausea and vomiting, and unsteadiness of gait. Ten months before entry, he sustained a slight head injury when he dived into shallow water. As well as he could remember, his head struck the bottom of the pool, but he was only dazed by the incident and had no difficulty in getting out of the water. The following day, his neck was sore and stiff, and there were pains at the base of his skull. When directly questioned about this symptom, he admitted to having had similar pains for at least 2 years prior to that time. From the date of the injury until admission to the hospital, the headaches became severer and more persistent. Anorexia, nausea and vomiting were frequent symptoms. Three months before admission, the patient fainted and was taken to a local hospital, where a physical examination and x-ray study of the cervical spine disclosed nothing abnormal. He began to have difficulty in walking, owing to stiffness and unsteadiness of his legs. Several times he became choked on food and had trouble drinking water. His speech had always been slurred. Weight loss had amounted to about 25 pounds and was attributed to the nausea and vomiting.

On examination, the blood pressure was 110/94, the temperature 98°F., the pulse 60, and the respirations 16. The patient was a tall, undernourished boy of asthenic habitus. The head and neck were held in a rigid posture but were well centered. He turned his body when looking to either side, and any sudden motion of the head was resisted, because of the pain thus produced. There was very slight but definite blurring of the optic-disk margins, and obliteration of the optic cups. The pupillary reflexes were normal, and ocular movements full. Jaw strength was good, and the sensation over the face was normal. Both sides of the face moved equally in mimicry and laughter. The jaw jerk was hyperactive. No disturbance of either division of the eighth cranial nerve was noted. Two days before operation, the patient

was unable to swallow either solid foods or liquids without choking. The sternomastoid and trapezius muscles were of good strength, but the tongue was weak and tremulous, though not atrophied. The speech was somewhat slurred but could have passed for normal. There was an unsustained and at times sustained horizontal nystagmus on both right and left lateral fixation of gaze. There was a slight terminal tremor in doing the finger-nose test, and the muscle tone in the arms seemed diminished. Tests of rapid alternating movements were done well. He tended to walk with a wide base and to deviate to either side. Heel-knee tests were performed with a minimum of unsteadiness. Sensation over the entire body was normal. The tendon reflexes were equal and slightly hyperactive; the abdominal reflexes were absent. There was urinary retention for 24 hours preceding operation.

The blood-cell counts and the urine were normal. Hinton and Wassermann reactions were negative on both serum and spinal fluid. The lumbar puncture showed *almost complete dynamic block*. Two days later, this was repeated with the same results. The total protein on the cerebrospinal fluid was 78 mg. per 100 cc.; the gold-sol curve was 0012210000, and there were no cells.

X-ray examination of the dural canal after lumbar injection of 5 cc. of lipiodol showed that the lipiodol could be freely moved through the lumbar and dorsal as well as the lower cervical spine. It met with obstruction at the upper edge of the 3rd cervical vertebra, the obstruction being cap shaped. The outline of the cap was hazy and not so distinct as that normally seen in complete obstruction of the spinal canal. No lipiodol was seen to pass beyond the obstruction during fluoroscopic examination of 10 minutes' duration, the patient being examined with his head hanging down at a tilt of 65°. Films taken 10 minutes later showed that some lipiodol had passed by the obstruction and lay in the interpeduncular cistern (Figs. 2, 3 and 4). The amount of lipiodol in the cerebral cavity increased during the next hour, although the patient stayed in horizontal position during this time. A definite upper edge of a tumor mass could not be demonstrated during examinations, which extended over 96 hours, although some lipiodol was constantly visible above the lesion when the patient was in the erect position. The conclusions were as follows:

The picture is very unusual. The obstruction with cap formation is in favor of a mass in the upper cervical area. There are, however, several features that are unusual for a tumor: the edge is not so distinct as one usually sees in tumor; the lobulation is more pronounced than that seen in tumor; an upper edge of the tumor is not demonstrable, although lipiodol is present above the area of obstruction; and the passage of lipiodol into the cranial vault is comparatively easy for a tumor of this size — there seems to be some kind of valve mechanism allowing the lipiodol to move with comparative ease upward into the skull but not downward from there into the cervical spine.

In spite of these unusual features, the preoperative diagnosis was tumor of the cervical cord, with extension into the posterior fossa.

At operation, performed by Dr. John S. Hodgson and Dr. W. Beecher Scoville, the dura was opened, and what appeared to be normal cerebellar tissue presented itself down to the level of the 3rd cervical vertebra. The arch of the foramen magnum, as well as the bone over the mid-occipital region, was removed, exposing the

cerebellum. The cerebellar hemispheres were small and atrophic and were situated high in the posterior fossa. From the lower portion of the cerebellum, there projected downward two parallel fingerlike processes that overlaid the dorsal surface of the medulla and upper cervical cord. These processes were densely adherent

and the overlying muscles and skin were closed without drainage.

The patient withstood the operation fairly well, although at the beginning he had a slow pulse and a respiration rate of 10 per minute. For the first hour after the operation, he had generalized muscular tremors. His



FIGURE 2. Case 1.

*Lateral view of upper cervical spine and base of skull after the head had been in dependent position for some time. The single arrows show obstruction of lipiodol column at a level that corresponds to lower end of prolapsed cerebellum. The double arrows indicate lipiodol which passed the obstruction and reached the interpeduncular cistern.*

both to the spinal cord and to each other. A large vessel with many branches filled the cleft between the two tonsillar projections. By measurement, the fingerlike projections extended a distance of 4 cm. into the cervical canal. An effort was made to pass a catheter between the processes and the cord so as to enter the 4th ventricle and aqueduct, but this proved impossible. Jugular compression was made, and normal spinal fluid oozed slowly from beneath and at the sides of the tonsillar projections of the cerebellum. The dura was left wide open,

convalescence proved to be slow and difficult. During the first 2 postoperative days, his respirations were slow (6 to 8 per minute), uneven and stertorous. Repeated inhalations of 5 per cent carbon dioxide in oxygen increased the rate to 14 per minute. Dysphagia was present for several days. Later he developed an acute epididymitis and an acute otitis media. Before discharge, films of the entire spinal column were taken and showed absence of spina bifida. On the 40th postoperative day, the patient was discharged. At that time his headaches

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in circumference (occipitofrontal). There was a scar over the spine in the lumbosacral region, and ptosis of both eyelids. Visual acuity, visual fields and optic fundi were normal. There was bilateral weakness of facial muscles, more marked on the right than on the left. Lateral conjugate deviation of eyes to both right and left was very poor. There was coarse, well-sustained syn-

gait was very ataxic. The only sensory loss was over the 5th lumbar and 5 sacral dermatomes, where all modalities were affected. Tendon reflexes were slightly hyperactive in the arms, but in the legs, knee jerks were diminished and ankle jerks were absent. Abdominal reflexes and extensor plantar responses were absent.

X-ray examination showed a large head and increased



FIGURE 4. Case 1.

*Anteroposterior view after the patient had been in horizontal position for some time. The single arrows indicate the lower edge of the protruding cerebellum; note its scalloped appearance. The double arrows represent lipiodol in the vault. 1 represents fillings in teeth; 2, the floor of the nasal cavity; and 3, the frontal sinuses.*

chronous nystagmus with the eyes at rest, which was increased by looking to either side or upward. Upward gaze was normal; convergence was poor. Speech was slurred, and there was slight dysphagia at times. There was weakness of hand grips, all movements of fingers and the flexors and extensors of the wrists. The interossei were atrophied, especially on the left. There was slight scoliosis to the left. Varus deformities of the feet, with weakness in dorsal and plantar flexion, were present. The

convolucional markings, and spina bifida in the lumbosacral region. Lumbar puncture revealed complete dynamic block on jugular compression, but good rise with abdominal pressure and cough. The spinal fluid, which had an initial pressure of 110 mm., was slightly xanthochromic; the total protein was 103 mg. per 100 cc., and the gold-sol curve 0000111000. A pneumomyelogram was unsuccessful.

While we were waiting to inject lipiodol into the spinal



canal and confirm the diagnosis of meningocele with Arnold-Chiari syndrome, the patient very rapidly became stuporous and soon was deeply comatose. An emergency operation, performed that night, consisted in suboccipital craniotomy and high-cervical laminectomy. A malformation of the hindbrain was found. The cerebellum projected into the cervical canal to the level of the second vertebra, and the medulla was displaced downward so that the cervical roots had to pass upward to where they made their exit through the intervertebral canals. Adhesions of the arachnoid and pia were very dense and were broken whenever possible. Convalescence was uneventful; the patient had no more headaches, the gait was improved, and when the patient was last seen in the Out Patient Department, 6 months after operation, the rest of the neurologic signs were stationary.

### DISCUSSION

These cases were clinically similar. In general, the symptoms can be classed under the following headings.

*Increased intracranial pressure.* Both patients, like many of those reported by Parker and McConnell,<sup>6,7</sup> had occipital headaches. Usually, the headache is occipital, suboccipital and cervical in location, comes on suddenly and is of several hours' duration, is aptest to occur during the night or in early morning, and sometimes causes a change in state of consciousness, such as fainting. The headache resembles in most respects the cerebellar-tumor headache. Both our patients had vomited with the headaches, and one was nauseated for several months. One patient had slight papilledema. Usually, the papilledema in this syndrome is not so marked as that in cases of cerebellar tumor.

*Involvement of several of the cranial nerves.* Sometimes the medulla is displaced so far into the spinal canal that the lower cranial nerves must pass through the foramen magnum to enter the cranial vault. Thus they are greatly stretched and often pinched as they go through the foramen magnum. Practically any one or several of the cranial nerves may show signs of injury, especially the lower ones. Our first patient had signs pointing to lesions of the seventh, ninth, tenth and twelfth cranial nerves bilaterally; the other had lesions of the third, seventh, ninth and, questionably, the twelfth.

*Compression of the brain stem.* The nausea and vomiting are usually attributed to medullary compression, as with cerebellar tumors. Other signs, such as disturbances of conjugate movements of the eyes and vertical nystagmus, are thought to be caused by intramedullary or intrapontine lesions.

*Compression of the spinal cord.* Both patients had bilateral pyramidal-tract signs; others have had

sensory disturbances. Of course, these signs could as well be due to compression of the brain stem. The marked weakness and atrophy of the hands in Case 2 is difficult to explain unless one postulates a small hydromyelia in the cervical cord. Other observers have found such lesions at necropsy.

*Cerebellar signs.* Symptoms suggesting cerebellar involvement may be the most striking part of the neurologic picture, or may consist of only slight gait disturbance, intention tremor or incoordination of movement.

Several neurologic conditions enter into the differential diagnosis of the Arnold-Chiari syndrome. Depending on whether the cerebellar symptoms, the cord symptoms or the intracranial-pressure symptoms are most marked, one considers cerebellar tumor, syringomyelia and syringobulbia, high cervical-cord tumor, — which extends through the foramen magnum into the posterior fossa, — intrapontine or intramedullary tumor, chronic adhesive arachnoiditis, cerebellar degeneration and platybasia. When the patient exhibits signs of a lesion involving several cranial nerves, the cerebellum, and the brain stem and of increased intracranial pressure, together with significant cerebrospinal-fluid findings (see below), most of the diagnostic possibilities are excluded. The neurologic diseases that should offer most difficulty in differential diagnosis are chronic adhesive arachnoiditis and platybasia.\* The latter is a deformity of the occipital bone and foramen magnum, and may produce pressure on the medulla oblongata and adjacent parts of the central nervous system, causing a clinical picture almost identical with the Arnold-Chiari syndrome. It is interesting to note that some degree of platybasia is often found in the Arnold-Chiari syndrome; in all probability it is an associated congenital anomaly of the skull. Nearly all the neurologic diseases considered in differential diagnosis lead to surgical exploration of the posterior fossa or cervical spinal canal; therefore, a diagnostic error is not serious.

Two laboratory procedures were found to be of diagnostic aid: lumbar puncture† and myelography. Lumbar puncture showed a complete block in the dynamics of cerebrospinal fluid, that is, jugular compression caused no rise in spinal-fluid pressure, although coughing, straining and

\*This congenital anomaly of the skull, also called "basilar impression," consists in an upward protrusion of the occipital bone around the foramen magnum, and is recognizable because major portions of the axis are above a line that connects the posterior edge of the hard palate with that of the foramen magnum.

†Caution should be taken in doing a lumbar puncture, because a very marked pressure change may cause medullary compression, thus endangering the patient's life. The information gained by this procedure probably justifies its careful use as a diagnostic measure but only after all other procedures are completed. Cisternal puncture is contraindicated.

abdominal pressure gave a prompt rise in pressure. The protein of spinal fluid was significantly increased. These findings are of course not specific for the Arnold-Chiari syndrome but only of a block in the cervical spinal canal. The intraspinal injection of lipiodol gives a very interesting and almost diagnostic picture, since it outlines the bifid projection of the two herniated cerebellar hemispheres.

The following description of the myelographic appearance of the protruding cerebellar tonsils seems to be characteristic of the lesion.

A mass within the upper cervical area produces a fairly marked block to lipiodol injected below the lesion. The block is less complete than one would expect from a tumor of similar size, the passage into the vault being less impaired than that in the reverse direction.

The outline of the mass is less distinct than that of tumor, owing to the sloping surface of the soft cerebral tonsils.

The edge of the mass shows lobulation produced by the gyri of the prolapsed cerebellum.

There seems to be a small central incisura within the mass corresponding to the incisura between the two cerebral tonsils.

Some degree of platybasia may be present.

A pneumomyelogram was attempted in Case 2, but was unsuccessful. In the future, this may replace the lipiodol method.

Most neurosurgeons have unsuccessfully operated on these patients. The patient often fails to regain consciousness or dies suddenly some time during convalescence, presumably from compression of the medulla. Probably the wise treatment is to decompress the cervical spinal cord and cerebellum but not to attempt to liberate the nerve structures in the posterior fossa from the arachnoidal adhesions. Any manipulation that causes a sudden change in the spatial relations of these structures may lead to death. Both our patients survived the operation, fortunately, even though more than a simple decompression was done. Pre-

operative ventricular drainage, as suggested by D'Errico<sup>9</sup> in the treatment of hydrocephalus associated with spina bifida, was not attempted.

#### SUMMARY AND CONCLUSIONS

The Arnold-Chiari malformation is a congenital anomaly in which the cerebellum and medulla oblongata are partially displaced into the spinal canal. Certain cases have an associated meningo-myelocele or platybasia.

Two cases of Arnold-Chiari malformation are reported, one with and one without meningo-myelocele.

The symptoms are divided into five groups: those due to increased intracranial pressure; to involvement of several of the lower cranial nerves; to compression of the medulla oblongata and pons; to compression of the spinal cord; to deformity of the cerebellum.

The differential diagnosis should include such possibilities as high cervical-cord tumor, cerebellar tumor, cerebellar degenerative disease, tumor of the medulla or pons, chronic adhesive arachnoiditis and platybasia.

Lumbar puncture gives confirmatory evidence of the protrusion of the inferior portions of the cerebellar hemispheres into the spinal canal, that is, increased protein and signs of dynamic block.

Röntgenographic examination after intraspinal injection of lipiodol demonstrates a highly characteristic picture of the pathologic process.

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## MICROCYTIC, HYPOCHROMIC ANEMIA, ASSOCIATED WITH SPLENOMEGALY AND REFRACTORY TO TREATMENT\*

### Report of a Case

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BOSTON

**I**N the course of observations on the hypochromic anemia of active rheumatoid arthritis, a thirty-nine-year-old Italian woman was encountered with a blood disorder characterized by severe hypochromia and microcytosis resistant to iron therapy, a blood smear showing basophilic stippling, polychromatophilia, target cells§ and marked anisocytosis and poikilocytosis, increased resistance of the red blood corpuscles to hemolysis in hypotonic salt solution, splenomegaly and an elevated serum bilirubin.

Wintrobe et al.<sup>1</sup> have recently reported a somewhat similar blood disorder in five persons over thirty-nine years of age, none of whom, however, had anemia of the severe degree shown by our patient.

The findings in our patient and in the members of her family are given below.

*The Patient.* J. A., a 39-year-old American-born Italian widow, was admitted to the Robert Breck Brigham Hospital in February, 1940, complaining of migratory, intermittent pain and swelling of the joints of 4 years' duration. Her father and mother were born in Italy and died in old age of a "stroke" and "ulcer of the leg" respectively. The past and system histories were not remarkable, except as presented in the present illness.

For 4 years, the patient had complained of painful swelling in the feet, ankles, knees, fingers and wrists. These symptoms seldom lasted more than a day and left no residual stiffness or disability; they were aggravated by wet weather and had recently become severe enough to interfere with her housework.

The patient stated that she had been "anemic" as long as she could remember. As a child, from about the ages of 7 to 10, she had "spleen trouble," at which time her abdomen was said to have been swollen periodically and to have become normal after the application of "plasters." Her older brother stated that she looked pale at that time, and that the family physician had said she had a very large spleen. These episodes, so far as the patient knew, were not attended by jaundice, chills, fever, nausea or vomiting. She had no more abdominal swelling after childhood. At the age of 8, she had a tapeworm of unknown variety, which was expelled after the administration of small pearl-like pills. She had never had any significant epistaxes, nor had she vomited any blood or coffee-grounds material. Bloody or tarry stools, hematuria, menorrhagia and metrorrhagia were absent, as were episodes of abdominal or back pain, vomiting, chills, fever

or jaundice. The patient had never had malaria. There was never a sore mouth or tongue, anesthetics or paresthesias; the appetite was good, and the bowel movements were regular, without diarrhea.

The patient had been a city-welfare case; she ate meat once or twice a week, but few colored vegetables or fruits and no whole-grain cereals, milk or eggs. Her alcoholic intake was very moderate. There was no history of exposure to benzol, lead, hair dyes, arsenic or commercial solvents. She never took cinchophen or other drugs for her joint pains, although she used acetylsalicylic acid occasionally for discomfort.

Physical examination showed a short, pale, somewhat stocky woman who appeared well and was in no great discomfort. The tongue was of normal color and not atrophic. The mucous membranes and conjunctivas were pale. The heart and lungs were normal. The abdomen was normal, except that the spleen was felt to descend on inspiration 3 cm. below the costal margin; its edge was very firm, nontender and smooth. The liver edge could not be felt. There was minimal periarticular thickening about the wrists and knees, and limitation of flexion of both little fingers. A neurologic examination showed normal reflexes and no sensory disturbances.

The blood showed a red-cell count of 4,300,000 with a hemoglobin of 7.9 gm. per 100 cc. of blood and a hematocrit reading of 30 per cent, and a white-cell count of 7600. A differential white-cell count was essentially normal. The blood smear showed marked variation in size and shape of the red cells, and there were a large number of microcytes, some well filled with hemoglobin. Many larger cells were markedly hypochromic. There were numerous pear-shaped and band-shaped, tailed, elliptiform and target cells. There were occasional cells showing polychromatophilia, and other cells with basophilic stippling. Smears at different times during hospitalization showed no normoblasts, but they were occasionally present (0 to 4 per 100 leukocytes) after the injection of epinephrine. Reticulocyte counts averaged 1 per cent. The platelets were normal to increased in number. Subsequent examination revealed that the color index was 0.51, the mean corpuscular volume 61.2 cubic microns, the mean corpuscular hemoglobin 15.9 micrograms and the mean corpuscular hemoglobin concentration 25.9 per cent. The serum bilirubin was 1.3 mg. per 100 cc., with an indirect van den Bergh reaction. A fragility test showed hemolysis beginning at 0.44 per cent saline solution, becoming definite at 0.28 to 0.32 per cent and complete at 0.12 per cent—a control showed beginning hemolysis at 0.44 per cent, becoming definite at 0.38 to 0.40 per cent and complete at 0.28 per cent. A test for urine urobilinogen with Ehrlich's reagent in serial dilutions of urine showed no urobilinogen beyond a dilution of 1:4 (control 1:8). Examination of wet films again showed the many bizarre forms seen in the smear, with many unusually flat irregular cells; there were no spherocytes. An anaerobic preparation failed to develop sickling of the red cells. No malarial parasites were seen.

\*From the Medical Service, Robert Breck Brigham Hospital.

†Formerly, student house officer, Robert Breck Brigham Hospital.

‡Research fellow, Robert Breck Brigham Hospital.

§Within the usually clear central area of the erythrocyte, there is a small island (bull's-eye) of hemoglobin, hence the resemblance to a target.

The serum protein, albumin globulin ratio, nonprotein nitrogen and fasting cholesterol were all normal. An analysis of fasting gastric contents showed 5 units of free and 6 units of total acid, after lusting, 82 units of free and 85 units of combined acid. The basal metabolic rate was -23 per cent, and following 2 weeks of therapy with 0.1 gm of thyroid daily was -12 per cent. Seven urine examinations showed nothing abnormal. Six stool examinations were negative for occult blood, and three revealed no parasites or ova.

During the patient's stay a sternal bone marrow biopsy

hyperplasia of normoblastic type, with a large increase in nucleated erythrocytes.

X-ray study showed bone changes consistent with mild rheumatoid arthritis. A skull plate was normal. There was no rarefaction or thinning of the cortex of the long bones. Thick and thin barium meals showed no gastric or esophageal varices or gastric or duodenal ulcer. A plain film of the abdomen showed the spleen to be enlarged.

During the patient's hospital stay and until August 13,

TABLE 1 Summary of Findings in J A and her Family

FINDINGS	J A					M F (DAUGHTER)	JUL A (DAUGHTER)	F S (BROTHER)	M A (BROTHER)	C H (SISTER)	
	2/16/40	3/11/40	4 7 5	40	8 13	40	4/25/40	8 14	40	4/30/40	6 26/40
Physical examination											
Jaundice	0	0	0	0		0	0	0	0	0	
Splenomegaly	++	++	++	++	++	0	0	0	0	0	
Lobulation	0	0									
Blood examination											
Erythrocytes (millions cu mm)	4.3	4.7	4.9	4.7		5.4	5.3	4.5	5.6	5.0	4.2
Hemoglobin (gm 100 cc)	7.9	7.5	3	3		12.2	11.3	11	13.1	9.5%	12.0
Hematocrit (%)	30	28	29			41	40	37	45		40
Color index		0.50	0.51	0.50		0.71	0.75	0.83	0.5		0.90
Mean corpuscular volume (cu microns)		61	58	56		73	4	61	81		95
Mean corpuscular hemoglobin (micrograms)		15	15	15		27	27	26	23		28
Mean corpuscular hemoglobin concentration (%)		25	25	27		30	33	31	25		30
Van den Berg (mg/100 cc)		1.3	1.1	1.7		1.1	0	0			0.3
Uterine index of plasma				11							
Reticulocytes (%)		1.7	1.3	1.8		1.0	0.8	1.0			
Abnormal erythrocytes											
Hypochromia	+++	+++	+++	+++		+	+	+	+		0
Anisocytosis	+++	+++	+++	+++		+	+	±	0		0
Poikilocytosis	+++	+++	+++	+++		±	+	±	0		0
Target cells	++	++	++	++		0	±	±	0		0
Polychromatophilia	++	++	++	++		±	0	0	0		0
Stippling	+	+	+	+		0	0	0	0		0
Nucleated red cells	0	0	0	0		0	0	0	0		0
Spherocytes	0	0	0	0		0	0	0	0		0
Frak tity test											
Hemolysis bu nse		0.36	0.44	0.47		0.44	0.44	0.38	0.44		0.40
Hemolysis dehnue		0.32	0.28	0.38		0.42	0.47	0.34	0.47		
Hemolysis complete		0.10	0.17	0.10		0.30	0.30	0.27	0.34		0.30

In the above table the following abbreviations are used: 0 absent ± rare + present ++ moderate +++ marked

was performed, and through the courtesy of Dr J Beach Hazard, reported as follows:

The marrow is of markedly increased cellularity, only about 10 per cent of fat cells being evident per field, as compared with the normal. Scattered megakaryocytes are present and appear in about normal number. The increase in cells is due for the most part to an increase in nucleated erythrocytes, either pyknotic or normoblastic. There is no increase in stem cells or megakaryoblasts. A differential count based on 600 cells is as follows: stem cells, 1 per cent; blasts, 10 per cent; nucleated red cells, 69 per cent (21 per cent normoblasts, 48 per cent pyknotic nucleated red cells), polymorphonuclear neutrophils, 10 per cent; polymorphonuclear eosinophils, 3 per cent; eosinophilic myelocytes, 5 per cent; and neutrophilic myelocytes, 2 per cent. Diagnosis: marked erythrocytic

1940, she was given in addition to thyroid, as above, ferrous sulfate, brewer's yeast, ascorbic acid and haliver oil. She received the routine orthopedic care, including postural exercises, occupational therapy, wax to her hands, Castex wristlets and beaver board under her mattress. Her course was uneventful. She was free from complaints soon after her arrival and was discharged in March. Since discharge, she has continued the therapy given during her hospital stay, but the blood findings have remained essentially unchanged from those at discharge (Table 1).

**The Patient's Children** M F, a 21-year-old married daughter, had always been well. A stained blood smear showed slight variation in size of the red cells, with occasional tailed or banded forms. A very rare macrocyte was seen, in addition to slight polychromatophilia. The remainder of the findings are shown in Table 1. This patient did not have her mother's blood disorder.

Jul. A., a 17-year-old daughter, had always been well. Her blood examination revealed a red-cell count of 5,370,000 with a hemoglobin of 12.3 gm. per 100 cc. and a hematocrit reading of 40 per cent. The color index was 0.75, the mean corpuscular volume 74.5 cubic microns, the mean corpuscular hemoglobin 22.8 micromicrograms and the mean corpuscular hemoglobin concentration 30.7 per cent. The smear showed slight but definite variation in size, and rare microcytes and band-formed, elliptiform, tailed and pear-shaped cells consistent with the degree of secondary anemia present. One target cell was seen in counting 200 white cells. The reticulocyte count was 0.8 per cent. There was no polychromatophilia or basophilic stippling. The differential leukocyte count was normal. A serum bilirubin was normal. A fragility test showed hemolysis beginning at 0.44 per cent saline solution, becoming definite at 0.42 per cent and complete at 0.30 per cent; a control blood showed identical hemolysis. Skull roentgenograms were normal.

Because of the blood smear and the degree of anemia, a course of iron therapy was given to discover if the changes in the stained blood smear were those secondary to a simple iron-deficiency anemia or related to the blood disorder of her mother. For 6 weeks, this girl took 0.7 gm. of ferrous sulfate daily, and examination of her blood at the end of that time pointed toward a simple iron-deficiency anemia (Table 1); there were fewer larger cells, better filled with hemoglobin, and the stained blood smear had changed slightly but definitely toward normal.

*The Patient's Brothers.* F.Y., a 54-year-old tavern keeper, had always been well. A stained blood smear was normal, and other laboratory studies (Table 1) were all within normal limits.

M.Y. had died, at the age of 49, of epidermoid carcinoma of the lung. Except for mild asthma and emphysema preceding his terminal illness, a gonorrheal infection and a head injury, his history was not remarkable. Only an admission blood was recorded during his terminal illness; it showed a red-cell count of 5,050,000 with a hemoglobin of 95 per cent (Tallqvist), as shown in Table 1. An autopsy was limited to the operative wound, and no bone-marrow samples were studied.

*The Patient's Sister.* Mrs. C.H., aged 52, had always been well; her blood was normal.

### DISCUSSION

From examination of the data, it can be seen that the patient suffered from a marked microcytic hypochromic anemia with a majority of microcytic hypochromic cells and, in addition, an impressive minority of macrocytic hypochromic cells with an irregular distribution of hemoglobin. There was evidence of marked bone-marrow activity, as indicated by the presence of polychromatophilia, basophilic stippling, normoblasts and young white cells. The increase of the young red-cell

elements after the injection of epinephrine, and the bone-marrow biopsy showing a profusion of normoblasts, confirmed this impression. There was a chronic mild bilirubinemia. The increased resistance of the red cells to hemolysis in hypotonic saline solution was consistent with the degree of microcytosis. In addition, the interesting history of splenomegaly in childhood and the long-standing symptomless anemia should be noted. The anemia was resistant to therapy, including large amounts of iron and extrinsic factors.

The family of the patient could not be shown to have this blood disorder.

The patient's blood disorder differed from Mediterranean anemia (Cooley's erythroblastic anemia<sup>2</sup>) only in lacking erythroblasts in the circulating blood and in roentgenographic changes in the bones. The latter may well be related to bone-marrow hyperplasia in growing bone.

This condition differs from familial microcytic anemia<sup>3</sup> because of absence of the disorder in other members of the family and the absence of skull changes with roentgen-ray study. In addition, our patient had splenomegaly, a permanently elevated serum bilirubin and a more abnormal stained blood smear.

The disorder appears to be similar to some of the cases described by Wintrobe et al.<sup>1</sup> It is also similar to the condition described by Dameshek<sup>4</sup> as "target-cell anemia," except for the absence of bone changes.

### SUMMARY

A case of hypochromic microcytic anemia, associated with splenomegaly and subclinical jaundice resistant to therapy, is presented, and its differences from previously described idiopathic anemias summarized. The erythrocyte changes bear marked similarity to those found in Mediterranean anemia in children.

### REFERENCES

1. Wintrobe, M. M., Matthews, E., Pollack, R., and Dobyns, B. M. A familial hemopoietic disorder in Italian adolescents and adults resembling Mediterranean disease (thalassemia). *J. A. M. A.* 114:1530-1538, 1940.
2. Cooley, T. B., Witwer, E. R., and Lee, P. Anemia in children with splenomegaly and peculiar changes in bones: report of cases. *Am. J. Dis. Child.* 34:347-363, 1927.
3. Strauss, M. B., Daland, G. A., and Fox, H. J. Familial microcytic anemia. *Am. J. M. Sc.* (in press).
4. Dameshek, W. "Target cell" anemia: anerythroblastic type of Cooley's erythroblastic anemia. *Am. J. M. Sc.* 200:445-454, 1940.

## NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FIFTIETH  
ANNIVERSARY

House of Delegates, May 12, 13 and 14, 1941

THE House of Delegates convened at the Hotel Carpenter, Manchester, on May 12, 1941, at 7 30 p m, with Speaker Robert O Blood, of Concord, presiding

The following members answered the roll call

The President, *ex officio*  
 The Vice President, *ex officio*  
 The Secretary Treasurer, *ex-officio*  
 I yall A Middleton, Plymouth  
 Richard W Robinson, Laconia  
 Francis J C Dube, Center Ossipee  
 W J Paul Dye, Wolfeboro  
 Norris H Robertson, Keene  
 Walter T Taylor, Keene  
 Leslie K Sycamore, Hanover  
 Everett C Crippbell, Woodsville  
 Frederic P Lord, Hanover (alternate for Willard A Bates, Littleton)  
 Deering G Smith, Nashua  
 Henry O Smith, Hudson (alternate for Charles H Cutler, Peterboro)  
 Clarence E Dunbar, Manchester  
 George V Fiske, Manchester  
 George C Wilkins, Manchester (appointed as alternate for Luther A March, Nashua)  
 Warren H Butterfield, Concord  
 Charles H Parsons, Concord  
 Herbert B Messinger, Franklin (alternate for Robert J Graves, Concord)  
 Martha I Boger-Shattuck, Portsmouth  
 James Sanders, Rye  
 Frederick S Gray, Portsmouth  
 Edna Walck, Dover  
 Albert E Barcomb, Rochester  
 Henry C Sanders, Jr, Claremont  
 William M Prince, Newport

The Speaker declared a quorum present, and appointed the Credentials Committee as follows Drs Dunbar (chairman), Dube and H C Sanders, Jr Dr Dunbar reported that the credentials were in order

The Speaker appointed the Committee on Officers Reports as follows Drs D G Smith (chairman), Sycamore and Robertson He appointed the Committee on Memorials and Communications as follows Drs Parsons (chairman), Beruoin and Middleton To the Committee on Nominations he appointed Drs Robertson (chairman), Robinson, Dunbar, Gray and Walck

The secretary treasurer, Dr Carleton R Metcalf, presented his report

*Report of the Secretary Treasurer*

The following report for 1940 is submitted

MEMBERSHIP, DECEMBER 31, 1940

PAID	
Belknap County	32
Carroll County	14
Cheshire County	31
Coos County	40
Grafton County	61
Hillsborough County	127
Merrimack County	71
Rockingham County	55
Strafford County	28
Sullivan County	19
Not in county society	5
	<hr/> 443

UNPAID	
Affiliate members	27
Honorary members	11
	<hr/> 38
Total	<hr/> 521

The total membership on December 31, 1939, was 526

## FINANCIAL STATEMENT

RECEIPTS	
January 1, 1940 — balance forward	\$1,210 84
Belknap County	192 00
Carroll County	90 00
Cheshire County	192 00
Coos County	276 00
Grafton County	372 00
Hillsborough County	781 00
Merrimack County	414 00
Rockingham County	336 00
Strafford County	180 00
Sullivan County	120 00
Cash received at annual meeting	42 00
Members not in county societies	30 00
Receipts from Bartlett Fund	2,000 00
Benevolence Fund (Women's Auxiliary)	225 00
New England Journal of Medicine subscriptions	6 00
Refund Cancer Commission	5 68
	<hr/> \$6,472 52
Net receipts from 1940 annual meeting, deposited 3/14/41	<hr/> 245 42
	<hr/> \$6,720 94

## EXPENDITURES

<i>New England Journal of Medicine</i> (journals)	\$614.73
<i>New England Journal of Medicine</i> (full subscriptions)	6.00
<i>New England Journal of Medicine</i> (transactions)	523.68
<i>New England Journal of Medicine</i> (half-tone cut)	1.28
Carleton R. Metcalf (salary)	400.00
Bridge and Byron (printing)	88.87
Envelopes, stamps and pamphlets	102.31
Eagle and Phoenix Hotel Co. (committee lunches)	16.15
Robert O. Blood (telegrams and telephone calls)	21.40
Robert O. Blood (clerical work, 1938-1940)	150.00
Women's Auxiliary	100.00
Benevolence Fund	477.00
Frank J. Sulloway (retaining fee)	100.00
Florence McCann (Committee on Education and Hospitals)	14.86
The Barwood Press (Committee on Education and Hospitals)	6.75
Dartmouth College (Committee on Education and Hospitals)	4.41
The Robbins Company (medals)	45.42
Concord Photoengraving Co. (half-tone cuts)	36.56
Frederic P. Lord (money allotted to General Fund)	1,000.00
Ernest M. Hopkins (gift, Dartmouth College)	2,000.00
Gray Service, Roosevelt Hospital (Dr. Mills's expenses at annual meeting)	39.00
C. F. Rhoads (expenses, annual meeting)	23.20
George C. Wilkins (Cancer Committee)	50.00
Leander P. Beaudoin (dues collected at annual meeting)	7.00
Deering G. Smith (dues collected at annual meeting)	35.00
Frederick S. Gray (dues collected at annual meeting)	7.00
Roy F. Plummer (primary expenses at Laconia)	100.00
John R. Perley (primary expenses at Laconia)	50.00
Deering G. Smith (expenses A. M. A.)	68.00
Madeline A. May (stenographer at annual meeting)	236.43
James B. Woodman (telephone calls)	12.55
Reliable Wiring Co. (lamp for index file)	14.24
National State Capital Bank (service charge)	1.00
	<hr/>
Balance in check book, April 5, 1941	\$6,352.84 119.68
	<hr/>
Net receipts from annual meeting deposited 3/14/41	\$6,472.52 248.42
	<hr/>
	\$6,720.94

The Society is in good financial condition, with a balance of \$119.68 in the bank on January 5, 1941. The Benevolence Fund on the same date amounted to \$2944.00; of this amount the principal is \$2594.19, and the accrued income, \$349.81. During the past year we have received \$225.00 for this fund from the women's auxiliaries of the following counties:

Strafford	\$50.00
Coos	10.00
Merrimack	25.00
Rockingham	40.00
Hillsborough	100.00

We gave \$100.00 to Mr. Frank J. Sulloway as a retaining fee, and \$100.00 to the Auxiliary to cover, in part, the expenses of its meeting last May.

Two officers of the Society have died during the past year: Osmon H. Hubbard, of Keene, and Fred E. Clow, of Wolfeboro. Both were members of the Advisory Committee on Jurisprudence. Dr. Hubbard was a former president of the Society, and Dr. Clow a former speaker of the House of Delegates.

The President chose David W. Parker, of Manchester, for anniversary chairman and appointed Harry O. Cheslev, of Dover, to membership on the New England Medical Council. The value of the New England Medical Council seems to me highly questionable. It has not had a meeting for years, and two or three years ago when we tried to get the different New England states to hold a meeting, Massachusetts was the only state that responded. It seems rather a futile gesture to appoint members to the council annually.

A year ago the House of Delegates made the following recommendations, which have been carried out:

Fifty dollars was given to the Cancer Committee for its work.

The members of the Society were urged to accord moral and financial support to the National Physicians Committee for the Extension of Medical Service.

A Committee was appointed to co-operate with the University of New Hampshire in celebrating its seventy-fifth anniversary.

I requested the chairman of the Committee on Officers' Reports and the chairman of the Committee on Memorials and Communications to send to each delegate an agenda of important matters to be taken up by delegates at this meeting.

Two thousand dollars was sent to Dartmouth College for use of the Medical School.

I conveyed to our United States senators the resolutions of the Society pertaining to the Wagner Act.

I conducted a postal-card ballot concerning the elimination or retention of round-table conferences at our annual meetings. The results were as follows:

*Do you prefer to return to the former plan of having members read set papers?* Yes, 44. No, 129. No answer, 10.

*If we return to the former plan, will you be willing to write and read a paper?* Yes, 54. No, 57. No answer, 64.

*Prefer present plan but will write a paper if former plan adopted:* 26.

*Prefer former plan and will write a paper if former plan adopted:* 25.

*Prefer neither plan but will write paper if former plan adopted:* 3.

There has been very little important medical legislation in the present session of the Legislature. I have appeared before a committee only once, to oppose the Federal Narcotic Bill, which contains a great deal of red tape and which would compel the State, at considerable expense, to carry on the work that is now being adequately done by the federal government. The bill was defeated.

The State Board of Health has requested us to appoint a Committee on Public Health to confer with them from time to time on matters in which they wish the opinion of the Society.

I shall be glad to have you instruct me in regard to

the action that I should take concerning doctors who are now or who will be in the United States Army. Should they be continued as members of the Society without payment of dues or should they be dropped from the rolls?

The President and I have had several meetings with General Bowen in regard to Selective Service. General Bowen requested us to choose doctors in various parts of the State to carry on the work of examining the draftees. We selected 176 doctors, and I am happy to say that every one of them agreed to serve without pay.

CARLETON R. METCALF, *Secretary-Treasurer*

Dr. Metcalf added that several other things should be mentioned: first, a communication from the Hartford Accident and Indemnity Company to the effect that, effective May 1, 1941, the annual rate for malpractice liability insurance for members of the Society had been reduced from \$40.00 to \$37.50 for the standard coverage of \$5000 to \$15,000; secondly, that \$1000 had been transferred from the General Fund to the Benevolence Fund; and, thirdly, that the expenditure of \$150 for political work in Belknap County seemed justified to the officers of the Society.

The report was accepted and was reported on by Dr. D. G. Smith, of the Committee on Officers' Reports. Dr. Smith spoke of the fact that several committee chairmen had failed to forward their reports to his committee in time for copies to be sent to the delegates; after some discussion, it was the consensus of the delegates that the chairmen should observe more strictly the regulation requiring the filing of reports by April 15.

Dr. Smith recommended that Article XII of the constitution, relative to the New England Medical Council, be deleted. (Action on this proposed amendment will be taken in 1942.)

Dr. Smith recommended that a standing committee, the Committee on Public Health, be appointed; after considerable discussion it was voted to table the question until the following day.

Dr. Smith recommended that the dues of members on extended active duty with the military and naval services of the United States be remitted for that calendar year in any part of which they are on active duty; it was so voted.

Because of the amount of business to be transacted, it was voted to omit the reading of the councilors' reports.

### *Reports of Councilors*

#### BEKNAP COUNTY

The Belknap County Medical Society held six meetings from November to April inclusive. The meetings were very well attended, some members driving over fifty miles to attend. As usual a dinner was served at 6:15, followed

by the program. The Women's Auxiliary met at the same time and place.

The society has thirty-seven members.

C. S. ABBOTT

#### CARROLL COUNTY

The Carroll County Medical Society has held its meetings at Center Ossipee as usual. The Auxiliary has held its meetings at the same time and place.

Our numbers are small, since our membership comprises but sixteen names; however our spirit is excellent and our meetings well attended.

C. E. SMITH

#### CHESHIRE COUNTY

The Cheshire County Medical Society held two well-attended meetings during 1940. At each meeting outside speakers presented papers of interest. These papers were given in such a way that much discussion followed. Discussions always stimulate interest and add to the value of such gatherings.

Three new members have been added to the society during the past year. This addition, however, did not swell our membership, since we lost three members by death: Dr. Hubbard, of Keene; Dr. Goldsmith, of Winchester; and Dr. Sheldon, of Troy. Dr. Goldsmith and Dr. Sheldon were fairly recent members, but by Dr. Hubbard's death the society lost one of its oldest members. Though quiet and unassuming, Dr. Hubbard had the faculty of accomplishing whatever he undertook. His activities in county and state medicine were many—to mention but a few, he had been president of the county society, president of the New Hampshire Medical Society, president of the staff of the Elliot Community Hospital and state pathologist.

JOHN J. BROSNIHAN

#### COOS COUNTY

We had no fall meeting this year. Our annual meeting was held in Berlin on April 26, 1941. The guest speaker was Dr. Henry Faxon, from the Massachusetts General Hospital, who gave us a very interesting talk on the subject, "Diagnosis and Treatment of Common Peripheral Vascular Diseases."

The society voted to let the Farm Security Administration function in our county.

We have forty-one members now, having lost two by removal and one by death. On the whole, our society is in a healthy condition.

We feel the loss of Dr. Homer Marks, who died on April 11, 1941, following an accident.

RICHARD E. WILDER

#### GRAFTON COUNTY

The annual business meeting of the society was held at the Hitchcock Hospital, Hanover, on October 30, 1940. President Ezra A. Jones, of the New Hampshire Medical Society, and Deering G. Smith, chairman of the New Hampshire Committee on Medical Preparedness, were present and led in the discussion of problems of medical preparedness. Dr. R. C. Tanzer, of Hanover, presented an interesting paper, "Special Problems in Plastic Surgery."

The spring meeting was held at the Hitchcock Hospital, Hanover, on March 28, 1941. It was voted to ap-



prove the plan of the Metropolitan Casualty Insurance Company for group disability insurance for members of the society. A sound motion picture, "Conception and Contraception," furnished by the Ortho Products Company, was presented.

The society has contributed to the support of the National Physicians Committee and has also contributed an emergency medical kit to the Medical and Surgical Relief Committee for Britain.

ARTHUR W. BURNHAM

#### HILLSBOROUGH COUNTY

The Hillsborough County Medical Society has had two meetings since the last annual meeting of the New Hampshire Medical Society.

On October 29, 1940, we met at the Manchester Country Club and the meeting was presided over by Dr. J. S. Black, of Nashua. At that time, six new members were admitted to the society; since then, two have been lost by death. At the business meeting a very interesting talk was given by Dr. Deering Smith, the New Hampshire delegate to the American Medical Association, on the subject, "Medical Preparedness." This was followed by much discussion. Remarks were made by Dr. Ezra Jones, president of the New Hampshire Medical Society, calling to our attention the fact that 1941 was the one hundred and fiftieth anniversary of the New Hampshire Medical Society. After luncheon, a paper was presented by Dr. Lyman G. Richards, of Boston. The topic of Dr. Richards's interesting paper was "Practical Bronchoscopic Diagnosis and Therapy," illustrated. Another paper of interest was by Dr. Joe Vincent Meigs, of Boston, and was titled, "Symposium on Vaginal Bleeding: Amenorrhea, dysmenorrhea and abnormal bleeding."

Our spring meeting was held in conjunction with the New Hampshire Surgical Club at the Nashua Country Club on April 29, 1941, with over a hundred physicians attending; Dr. George T. Sheehan, president of the society, presided.

The scientific program of this meeting included surgical clinics at St. Joseph's and Memorial hospitals and papers on the following subjects: "The Treatment of Toxemias of Pregnancy," by Dr. Marion Fairfield; "Peritonitis," by Dr. Loren F. Richards; "Middle-Ear Infection," by Dr. Raymond Marcotte; and "Large Inguinal Rings as a Bar to Employment," by Dr. Richard Mulvanity. During the afternoon Dr. Joseph W. O'Connor, of Worcester, Massachusetts, presented a very interesting paper, "Spontaneous Rupture of the Uterus: Its diagnosis and treatment." He was followed by Dr. John M. Birnie, of Springfield, Massachusetts, who gave an excellent presentation on the subject, "Large Inguinal Rings and Potential Hernias." Both of these were discussed by members of the society and the club, and then followed a motion picture, "Vitamin B Deficiencies and Their Treatment," shown by E. R. Squibb and Company.

Of the 179 physicians in Hillsborough County, 140 are members of the Hillsborough County Medical Society. Several new members were admitted at this meeting. Four of our members, Dr. R. E. Fiske, Dr. G. J. Kapopoulos, Dr. R. M. Bremner and Dr. D. L. Hallisey, are on active duty with the National Guard. There are eight medical reserve officers in the county, of whom Dr. M. O. Goodman, Dr. P. R. Hamel, Dr. R. E. Lapointe and Dr. R. R. Rix are on active duty for a year.

The accident and health insurance plan which was proposed to our members at the last meeting and approved

by them has gone into effect, over half the eligible members taking out policies.

CLARENCE O. COBURN

#### MERRIMACK COUNTY

A summer meeting was held at Franklin at the Country Club on July 10, 1940. About twenty members attended. Dr. Levine, of Bristol and Concord, gave a paper on superstitions relating to medical treatment in the early New England period. A local county defense committee, consisting of Dr. McQuade, of Franklin, Dr. MacLean Gill, of Concord, and Dr. Warren Butterfield, of Concord, was elected.

At the fall meeting, held on October 2, 1940, at the Eagle Hotel, Dr. Deering G. Smith discussed the defense program and the part the medical profession will have in it.

On January 8, 1941, the following officers were elected: president, Dr. MacLean J. Gill; vice-president, Dr. Edward Putnam; secretary-treasurer, Dr. Warren Butterfield. Mr. Davis, of Nashua, and Manager L. F. Carter, of the Metropolitan Casualty Company, presented a plan for health and accident insurance for the members of the society. A motion was made and passed to accept this insurance plan and to authorize the committee of five to make the necessary arrangements.

On April 2, 1941, a noon meeting was held at the Eagle Hotel; about twenty-five were present. The Orthogynol Company presented a motion-picture film with sound track, "Studies in Human Fertility: Methods for the control of conception."

HENRY H. AMSDEN

#### ROCKINGHAM COUNTY

Rockingham County Medical Society has held two meetings during the past year, the spring meeting at the Portsmouth Hospital and the fall meeting at the Exeter Hospital.

At these meetings, cases were presented showing end results. At the fall meeting, a paper was read by Dr. Robert Zollinger, of Boston. At the spring meeting, Dr. Ezra Jones, of Manchester, talked on various difficulties in treating many types of fractures and Dr. A. Peters discussed the use of lipiodol in determining the patency of the fallopian tubes by x-ray. The meetings were very interesting, instructive and well attended.

HERBERT L. TAYLOR

#### STRAFFORD COUNTY

The Strafford County Medical Society has twenty-nine active members and six affiliate members. Two applications for membership were acted on at the April 30, 1941, meeting.

The annual meeting was held on October 30, 1940, at the City Hotel in Rochester. It was the one hundred and thirty-third meeting of this society and was attended by twenty-five members and one guest. Dr. Deering Smith, chairman of the State Committee on National Defense, spoke on the American Medical Association's plan to register all physicians in the United States and on their place in the national defense program. During the winter and early spring months, every physician in Strafford County was registered in accordance with this program.

Our spring meeting was held on April 30, 1941, at Simpson's Pavilion in Dover, with twenty-two members

and two guests present Dr Chester S. Keefer, of Boston, spoke, his subject being The Modern Treatment of Pneumonia. Considerable business was transacted, which included voting two new Rochester physicians to membership, voting Dr A. P. Richmond, formerly of Dover to honorary membership, appointing a committee to study the so-called Houston Plan, a vote against any change in the present Cancer Commission and telegrams of such action sent to the secretary of the New Hampshire Medical Society and to Winslow Osborne, chairman of the Committee on Revision of Statutes, State House, Concord presentation of Group Health and Accident Insurance for Physicians, which was favorably accepted. This was the most active meeting we have had for some time.

During the year 1940 one member was lost by death—Dr L. L. Gilman, of Rochester, who died on April 12, 1940, at the age of seventy-one. Dr Andrew J. Oberlander, formerly at New Hampshire University accepted a position with an insurance company and moved to Burlington Vermont. Dr L. H. Mendelson formerly of Dover, removed to Winchester. Dr Dean Wilder Dr Oberlander's successor at New Hampshire University went to Derry to become a general practitioner.

Dues of all the members were paid promptly and disbursed to the state society treasurer on February 6, 1941.

JOHN A. HUNTER

#### SULLIVAN COUNTY

The Sullivan County Medical Society held two meetings during the past year. The summer meeting was held at Seven Hearths, in Sunapee, and consisted of a luncheon followed by a scientific session, at which Dr Ralph E. Miller, of Hanover, talked on laboratory technique and the need of laboratory examinations in general practice, particularly stressing frequent blood sugar determination in the treatment of diabetes.

The winter meeting was held at Claremont. At this time officers were elected for 1941. The speaker was Dr George S. Amsden, of Alstead, who gave a very interesting and instructive talk on the neurologic patient. We had hoped to have our state society president at this meeting and were much disappointed that he could not attend.

We are pleased to report the Sullivan County Society in a very healthy condition.

EMERSON M. FITZGIB

Dr D. G. Smith then made his report as delegate to the American Medical Association.

#### *Report of the Delegate to the American Medical Association*

The ninety-first annual session of the American Medical Association, held in New York City, June 10-14, 1940, was the best attended medical meeting that has ever been held, the total registration being 12,864, more than 2500 greater than any previous session. Thirty-nine New Hampshire doctors were registered, and your delegate served as sergeant at arms at the meetings of the House of Delegates. The secretary reported the membership of the American Medical Association to be 116,266, an increase of 15,000 members in five years, which is proof of the solidarity of the medical profession. Dr Rock Sleyter, the president, remarked on how little the average doctor knows about the association and what it is doing. He recommended the training of speakers who could appear on the programs of the various county societies to bring

home to the doctors the activities and policies of the American Medical Association.

The House of Delegates recommended to all state medical societies that they hold conferences with the authorities of their state boards of health, with the view of limiting the type and extent of services offered by the laboratories of these organizations. Laboratory services by the state board of health laboratories should be confined to requests made by health officers and to those made by physicians whose patients find it difficult or impossible to pay the cost of laboratory services of this kind in the customary manner. In general, laboratories of the state boards of health should not provide services at taxpayers' expense to persons who are able to provide for themselves.

The by-laws were amended by creating a new section of the scientific assembly, the Section on Anesthesiology. It was also proposed to amend the constitution so that only doctors of medicine licensed to practice medicine and whose licenses are registered in the state or county in which they make application be accepted for full membership in the American Medical Association. The determination on the part of the Board of Trustees to use every effort and means to defend the American Medical Association against the charges that it is guilty of conspiracy and of violating antitrust laws received the wholehearted endorsement of the House of Delegates. New England was honored by the choice of Frank H. Lahey, of Boston as president elect.

Medical preparedness was the major topic discussed at the meetings of the House of Delegates. Colonel George C. Dunham submitted a tentative plan for the procurement of professional personnel for the Medical Corps of the United States Army in the event of a national emergency. This plan was prepared by the office of the Surgeon General of the United States Army and was endorsed in principle by the House of Delegates. The House of Delegates created the Committee on Medical Preparedness, which is to establish and maintain contact and suitable relationship with all governmental agencies concerned with the prevention of disease and the care of the sick, in both civil and military aspects, so as to make available at the earliest possible moment every facility that the American Medical Association can offer for the health and safety of American people and the maintenance of American democracy.

The president and secretary of the New Hampshire Medical Society were asked to recommend a chairman for this state. Following their recommendation, Dr Deering G. Smith was appointed New Hampshire chairman by the Committee on Medical Preparedness of the American Medical Association. Dr Smith chose Dr L. A. Jones and Dr Carleton R. Metcalf to serve with him on the state committee. On the suggestion of the state chairman, the president and secretary of each of the county societies appointed medical preparedness committees in their counties.

At the request of the Surgeons General of the United States Army, Navy and Public Health Service, a questionnaire was sent to every licensed physician in the United States in order to have an inventory of the doctors and their capabilities. The county medical preparedness committees have cooperated in getting doctors to complete these questionnaires and blanks have been returned for every doctor in this state. The information on these questionnaires has been copied onto punch cards so that it is possible by the use of the usual machines to pick out any special group of physicians.

The carrying out of the Selective Training and Service Act of 1940 necessitated the use of physicians as examining physicians of the draft boards and as members of the medical advisory boards. The president and secretary of the Society made recommendations of doctors to the Governor, who nominated the physicians for the President to appoint, and who appointed the members of the medical advisory boards.

It was found necessary to use some civilian physicians for the final examinations for the United States Army. Volunteers were asked to serve on the medical induction boards, and over thirty physicians answered this call.

Dr. Smith spoke on medical preparedness at a majority of the county medical meetings in the fall, has attended several conferences, and has directed this work in the State. Every effort is being made to provide for the medical care of the United States Army and at the same time to look after the needs of civilian hospitals and of cities and towns, especially to prevent the stripping of rural and isolated communities of their necessary medical personnel. Information has been sent to the Corps Area Surgeon as to which medical reserve officers may be spared for active duty at this time and which officers should remain at home to take care of the needs of the community or its hospitals. At the present time each county medical preparedness committee is making a similar report about the other physicians in its county. The names of physicians who are deemed essential for the medical staffs of hospitals and related institutions, health departments and medical schools are being listed, and also the names of physicians who are needed for full-time industrial practice and for the care of the civilian population.

Eight New Hampshire doctors are now in active federal service with the National Guard, and at least sixteen other doctors are now serving a year's active duty as medical reserve officers. The practices of these physicians and of physicians who will subsequently go into the military service should be protected, and the House of Delegates recommended to the constituent state and component county societies that they work out plans whereby the practice of physicians absent from their homes in the service of our military and naval forces be protected, and whereby some financial return from such practice be secured for the physicians so absent in the service. Your delegate recommends that this matter be referred for study and action to the Committee on Medical Economics.

It is suggested that a committee on medical preparedness be chosen by this society, so that no question of authority may arise when we are dealing with the state and federal governments.

Your delegate appreciates the excellent work that the examining physicians of the draft boards and the members of the medical advisory boards have been doing. He has had the full co-operation of all the doctors of the State, and especially thanks the members of the medical preparedness committees for their assistance.

DEERING G. SMITH

As chairman of the Committee on Officers' Reports, Dr. D. G. Smith recommended that the part of his report dealing with medical defense should be read at the general meeting of the Society; it was so voted. After some discussion, the recommendation that the Committee on Public Health be instructed to study the problem rel-

ative to the State Laboratory as a real competitor of the clinical pathologists was laid on the table indefinitely. Dr. Smith's recommendation that the matter of protection for the practices of members who left the State because of military or naval service be referred to the Committee on Medical Economics for study and action was approved, as was the suggestion that a committee on medical preparedness be created, the suggestion being made that the New Hampshire Committee on Medical Preparedness of the American Medical Association constitute this new committee of the Society.

Dr. Woodman then presented the report of the Committee on Amendments to the Constitution and By-Laws.

### *Report of the Committee on Amendments to the Constitution and By-Laws*

The Committee on Amendments to the Constitution and By-Laws met on March 31, 1941, and compared our constitution and by-laws with those of the American Medical Association. Owing to the excellent work of Dr. H. O. Smith and his committee, we find no discrepancies. We make the following recommendations:

1. It is recommended that, in Chapter VIII, Section 1, of the by-laws, the Nominating Committee be stricken from the list of standing committees. This committee is a special committee appointed for a special purpose and is provided for in Chapter V, Section 2, of the by-laws.

2. It is recommended that, in view of the above, Chapter VIII, Section 2, of the by-laws be stricken out entirely.

3. It is recommended that the list of standing committees shall include a committee on child welfare and maternal health.

4. It is recommended that a section be added to Chapter VIII defining the Committee on Child Welfare and Maternal Health as a committee consisting of three members whose duties it shall be to investigate the condition of child welfare and maternal health throughout the State, to report to the Society the cause of maternal and infant mortality and morbidity and to recommend any course of treatment or method of procedure that would improve such existing conditions.

5. It is recommended that each county society shall compare its constitution and by-laws with those of the state society and see that no conflict exists.

JAMES B. WOODMAN  
CHESTER L. SMART  
FREDERICK S. GRAY

Dr. D. G. Smith, acting for the Committee on Officers' Reports, approved the recommendations and proposed the following changes in the by-laws:

1. Chapter VIII, Section 1: strike out "A Committee on Nominations."

2 Chapter VIII strike out Section 2

3 Chapter VIII, Section 1 add a Committee on Maternal Health and Infant Welfare after a Committee on Medical Education and Hospitals

4 Chapter VIII renumber Sections 3 to 12 inclusive, making Section 3 Section 2 and so forth

5 Chapter VIII add a new section Section 17 as follows

The Committee on Maternal Health and Infant Welfare shall consist of three members whose duties it shall be to investigate the condition of maternal health and infant welfare throughout the State and to report to the Society the causes of maternal and infant mortality and morbidity and to recommend any course of treatment or method of procedure which would improve such existing conditions

The committee also recommended that, if the amendments were adopted, the Committee on Maternity and Infancy should be abolished. Since no action could be taken, the proposed changes were tabled until the next meeting. However, it was voted that it was the sense of the meeting for the Committee on Maternal Health and Infant Welfare and the Committee on Child Health to be standing rather than special committees.

Dr Wilkins then presented the report of the Committee on the Control of Cancer

### *Report of the Committee on the Control of Cancer*

During the past year your committee has sent out three letters to every physician in New Hampshire. These one page letters have dealt with three phases of cancer control.

The first was a quotation on cancer education for the physician, which was written by Dr C C Little, the director of the American Society for the Control of Cancer. This letter dealt with the accomplishments in my education that had been directed toward informing the public of the danger signals of cancer and an attack on fear of the disease. The unreasonable fear of cancer and discussion of it have been controlled to a considerable degree and the education of the public has reached a point where there is definite need for further medical education although this need varies in different states and communities.

The second letter dealt with the necessity of examining patients who have abnormal flowing even though the flowing is present at the time of the visit to the doctor. Too many patients have remained away too long a time when told to return when flowing ceased. Physicians were also urged to encourage women to have a vaginal examination between the ages of thirty five and forty and to advise cauterization and repair of cervical erosions when discovered. The importance of periodic examinations was also stressed in this letter.

In the last letter, yearly physical examination was stressed more fully, and certain diagnostic procedures were discussed that should be observed in making an examination. Your committee believes that if these rules were followed in all physical examinations very few early cancers would be overlooked in the patients thus examined.

Here in New Hampshire we believe that the medical profession is constantly growing more alert in recognizing conditions that may indicate the possibility of cancer and reports from the various diagnostic clinics in the State bear out this assumption since more and more physicians

are sending patients to the clinics for assistance in making definite diagnoses. The important educational work of the Women's Field Army continues, and through its efforts, hundreds of women have become interested in cancer control and through their efforts thousands of pamphlets giving information in simple language have been distributed to homes throughout the State. These women as a group have many times praised the assistance and co-operation of the physicians in their communities.

Last July the Women's Field Army donated funds for the purchase of about six hundred copies of the book *Cancer Manual for Practitioners*. One of these volumes was sent to every member of the Society. We assume that every physician receiving this most informative book appreciated it although the Women's Field Army had only ten letters of thanks.

New Hampshire is a small state, most of our physicians are intelligent and alert and the New Hampshire Medical Society is a fairly compact group hence your committee believes that there is no reason why the medical profession of this state should not lead other states in its ability to recognize cancer early and see that patients receive early and competent treatment. Your committee will gratefully receive any suggestions of further means and methods by which our educational efforts can be improved.

The committee has spent \$42.57 for printing and postage the balance of \$7.43 having been returned to the Treasurer. We request another appropriation of \$50 for the coming year.

GEORGE C. WILKINS

On the recommendation of Dr D G Smith, of the Committee on Officers' Reports, the appropriation of \$50 for the work of the cancer committee and the sending by the Secretary of a letter to the Women's Field Army expressing gratitude for the forwarding of copies of the cancer manual to all members of the Society were approved.

The report of the Committee on Medical Economics was read by the chairman, Dr Robinson.

### *Report of the Committee on Medical Economics*

The Committee on Medical Economics has continued the activities reported at the last annual meeting and presents the following report on the problems it has considered.

*Medical Care for Clients of the Farm Security Administration*—This program was in effect in Grafton and Cheshire counties for the full year of 1940. It appears to have worked out in general to the satisfaction of both the patients and the physicians concerned. All bills submitted by the participating physicians during the year were paid in full. Repayment of loans made to clients by the Farm Security Administration was in the neighborhood of 90 per cent, a fact indicating that in the majority of instances the program is fulfilling its original purpose of maintaining the self-sufficiency of the participating clients and has not degenerated into a government subsidy. The plan is being continued in Grafton and Cheshire counties for the year 1941. The prospects for successful operation are somewhat more uncertain this year since shifting economic conditions are causing migration of labor from farm to industry and the number of families participating will probably be smaller than that of last year. Your committee will continue its observation of the

operation of the program, and makes no specific recommendations at the present time.

*National Physicians Committee for the Extension of Medical Service.* This committee has done valuable and effective work during the past year in interpreting the aims and ideals of the medical profession to the public, and in combating undesirable trends toward government interference in the practice of medicine. Since it is a vital concern of physicians today that the public be educated to a sympathetic understanding of their position, and since the National Physicians Committee appears to be an effective and ethical agency for the attainment of this purpose, your committee recommends the continued moral and financial support of the committee, both by physicians individually and by the county and state societies. Specifically, it is recommended that the state and county societies make use of the news releases furnished by the National Physicians Committee for insertion in local newspapers.

*Group Sickness Insurance.* Your committee has continued its study of various plans now in effect for group insurance against the costs of medical care. It has considered the advisability of a fact-finding survey of conditions in New Hampshire, but has concluded that it would be useless to conduct such a survey at the present time, in the face of rapidly changing economic conditions. Furthermore, it is the opinion of your committee that with the expanding opportunities for employment that exist at present and will probably continue to exist for some time to come the need for group insurance against the costs of sickness is less acute than it has been in the recent past. Your committee believes, however, that the New Hampshire Medical Society should be prepared to introduce such a program if and when it should seem desirable in the future. Since a prerequisite of any such program would be the passing of an enabling act by the Legislature, it is recommended that the Committee on Public Relations or the Committee on Medical Economics be instructed to consult with Attorney Sulloway with the purpose of drawing up such a bill for later submission to the Legislature.

RICHARD W. ROBINSON, *Chairman*  
CLARENCE E. DUNBAR  
LESLIE K. SYCAMORE

Dr. D. G. Smith, for the Committee on Officers' Reports, expressed gratification that the plan for the medical care for clients of the Farm Security Administration was in successful operation, approved the work of the National Physicians Committee for the Extension of Medical Service, and urged that the news releases of the latter organization be used by the secretaries of all state and county medical societies. He recommended that the Committee on Public Relations and the Committee on Medical Economics consult with Mr. Sulloway relative to enabling legislation for group insurance against the costs of medical care and report back to the House of Delegates at its next annual meeting; after some discussion, the motion was passed.

The report of the Committee on Medical Education and Hospitals was then presented.

## *Report of the Committee on Medical Education and Hospitals*

### POSTGRADUATE MEDICAL EDUCATION

The New England Postgraduate Assembly will hold its fourth annual session in October on dates which will not be in conflict with any state medical society meeting or other major medical function. On the recommendation of your representative, the emphasis in the program will be from the viewpoint of the general practitioner.

A preliminary program will be issued this spring under the direction of the co-chairmen, Drs. Chester S. Keefer and Joseph H. Pratt, for medicine, and Drs. Howard M. Clute and William E. Ladd, for surgery. The success of the previous programs is a guarantee of the value of the next. An attendance of eight hundred, a modest expectation from the five states, will assure the necessary income for expenses, thus obviating underwriting by the Society. Each member should begin now to formulate plans permitting attendance.

At the fourth annual session of the Associated State Postgraduate Committees held in New York City on June 12, 1940, the new chairman, Dr. Frank R. Ober, of Boston, appointed a committee to study a proposed national registry of postgraduate instructors and meetings. The New England member is Dr. Frederick T. Hill, of Waterville, Maine. In the meantime an interstate mailing list has been established, permitting a nation-wide exchange of information, which is especially important in these days of constant scrutiny from without and within that call for continual alertness in how to provide the best grade of medical service for the protection of public health in the national interest, in which postgraduate instruction is a most significant factor.

### COMMONWEALTH FUND FELLOWSHIPS

Postgraduate medical education in our own society has been significantly influenced in the past half decade by the fellowships provided by the Commonwealth Fund. It seems appropriate at this time to present a summary of these because of their importance as historical evidence of trends in the State, and because the bare numbers might appear to constitute something of a challenge to a certain age group in the Society when considered in the light of the fact that almost without exception the applicants who have been out of medical school five years and who have not been more than forty-five years of age have received awards within the limits of the fellowships available for any particular year.

It might be considered, on the other hand, from the basis of the same bare numbers that the Society has made a very respectable showing. It would be impossible to determine exactly how many fellowships under their specifications the directors of the Commonwealth Fund might have awarded during the period assuming an unlimited supply, but a statistical study discloses that somewhere between one fifth and one third of all those who might have been eligible did receive fellowships.

Sixty fellowships were awarded to thirty-seven of forty-two applicants; twenty-one fellowships were single, while ten awards were double. Five physicians received three grants, and one received four. Over half (thirty-three) were in medicine, ten in obstetrics, eight in pediatrics, seven in surgery, and two in x-ray. Two took medicine twice, and one each repeated pediatrics and x-ray.

In 1936 there were eight, in 1937 fourteen, in both 1938

and 1939 eleven, and in 1940 sixteen applications, in contrast with six for 1941. Each year new eligibility comes into existence and older practitioners are still considered on the basis of their individual qualifications. The directors of the Commonwealth Fund have shown a broad and most intelligent understanding of the problems of practice in the State, and it is to be hoped that our members will express their appreciation by continuing to take advantage

of this opportunity of maintaining to an increasing degree a high level of professional competency.

JOHN P. BOWLER, *Chairman*

JAMES W. JAMESON

HERBERT L. TAYLOR

(To be continued)

## MEDICAL PROGRESS

### THE TREATMENT OF DEGENERATIVE JOINT DISEASE\*

CHARLES L. SHORT, M.D.,† AND WALTER BAUER, M.D.‡

BOSTON

AS WILL be noted by the title, we prefer the term, "degenerative joint disease," to any of the more commonly used synonyms: hypertrophic arthritis, osteoarthritis or senescent arthritis. Our reasons for this choice are, first, because it is now generally agreed that degeneration of the articular cartilage is the primary pathologic change<sup>1-15</sup> and, secondly, because true arthritis, which suggests inflammation and even infection, is very rarely present.

Degenerative joint disease is without doubt the commonest articular disorder. All persons beyond the second decade of life, although they may not complain of skeletal symptoms, exhibit anatomic alterations in their joints similar to the pathologic changes observed in this disease. The agent responsible for this articular lesion has a scope of unusual width, as indicated by the facts that many animal species<sup>4, 8, 12</sup> in dissimilar geographic locations and persons of both sexes are affected, and that not only the articular coverings but also the hyaline cartilage in various sites of the organism participate in the characteristic changes. Although sequelae identical to degenerative joint disease may supervene on the subjection of articular cartilage to a great variety of pathologic influences,—such as trauma, disturbed joint mechanisms and inflammatory joint disease,—there remain a very large number of cases of this disease in which no such factor appears to have been operative. Regardless of etiology, however, two fundamental considerations apply to every example of degenerative joint disease. One is the disadvantageous biologic position of the articular cartilage when it meets with injury; this is evident, anatomically, in the paucity of its cellular constituents and in its remoteness from blood supply and, physiologically, in its low respiratory rate and in its extremely limited faculty of autogenous repair.<sup>16</sup> The other concerns the effect of mechanical stress and strain incident to joint function on a tissue whose specific means of resistance to such use has been depleted. It is this second group of forces that plays the dominant role in the localization and progression of the arthropathy to the late and conspicuously deforming changes. The most constantly observed correlative to the so-called "primary form" of degenerative joint disease is increasing age. This has been well demonstrated in a recent report.<sup>15</sup> From this study, it is apparent that further knowledge concerning the cause and prevention of this articular lesion depends on precise data concerning the factors that govern maturation, maintenance and senescence of hyaline cartilage and other mesenchymal tissue. The best chance of obtaining this much-needed information resides in the development of better staining technics, the combination of microscopic observations and histochemical methods, and studies in tissue metabolism.

Those who have the misfortune to acquire pain and disability as a result of their degenerative joint-disease changes can be divided into two groups. In the first group, which might be termed the "primary or endogenous type," a factor as yet unrecognized is at work. In the remainder, which we may call the "secondary or exogenous type," long-continued trauma is the agent that oftentimes favors the development or acceleration of hyaline-cartilage degeneration. The various agents that may be operative and a knowledge of which is of value in reference to the

\*All articles in this series will be published in book form; the current volume is *Medical Progress: Annual, 1940* (Springfield, Illinois, Charles C. Thomas Company, 1941. \$4.00).

†From the Medical Clinic, Massachusetts General Hospital, the Department of Medicine, Harvard Medical School, and the Massachusetts Department of Public Health.

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The expenses of this investigation were defrayed, in a large part, by a grant from the Commonwealth Fund, New York City.

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treatment and to the prophylaxis of this condition are as follows: long-continued trauma, such as that in occupations demanding persistent use of one or more joints and that in obesity, in which the weight-bearing joints are subjected to unusual strain; static deformities resulting from severely pronated feet, knock-knees or bowlegs, poor posture (with obesity often a factor), fractures healing with malalignment, displaced patellas, incompletely healed sprains or unreduced dislocations or diseases of the epiphysis; and intra-articular disease, previous or present, which is the result of trauma (including osteochondritis dissecans, internal derangements of the knee joint, fractures into the joint and so forth), sepsis (joint infections due to the gonococcus, pyogenic organisms and so forth), gouty arthritis or rheumatoid arthritis.

It is thus apparent that degenerative joint disease may follow many types of articular injury and may often represent the end stage of other types of arthritis. Accordingly, the physician should not be satisfied with a clinical or roentgenologic diagnosis of this condition without first ascertaining whether one of the above-mentioned factors is of causative importance. Furthermore, he must make certain that the degenerative changes are actually responsible for the patient's symptoms, and that they are not merely a coincidental finding.

The onset of degenerative joint disease is usually gradual and the course chronic. Differentiation from the various acute and chronic arthritides is rarely difficult. As previously pointed out,<sup>17</sup> it is of extreme therapeutic and prognostic value to distinguish degenerative joint disease from rheumatoid arthritis. Patients showing evidence of both diseases should not be given the diagnosis of mixed arthritis. It is the physician's duty to decide whether the two diseases occupy a causative or a coincidental relation.

Since articular cartilage, because of its physiologic limitations, has a limited ability to repair itself, anatomic cure of degenerative joint disease is not possible. On the other hand, treatment directed toward the correction of causative or accelerating factors (if present and reversible) will arrest the progress of the disease and, in conjunction with simple measures to be described, will relieve the patient's symptoms.

Articular cartilage itself is insensitive. The pain in degenerative joint disease is therefore due to secondary changes, including muscle spasm caused by mechanical strain, loose bodies, secondary inflammation of fibrous tissue or bursae and elevation of the periosteum from the marginal overgrowth of cartilage and bone. The first three may be relieved by treatment, notably rest and re-

moval of irritating factors, and the last tends to subside when proliferation of cartilage ceases and calcification takes place. The most easily observed example of this process is seen in degenerative disease of the terminal phalangeal joints (Heberden's nodes), which often begins as a tender painful swelling that, in the course of a few months, becomes ossified and relatively painless. This tendency to self-limitation must be recognized in the evaluation of any form of therapy and has undoubtedly led to false claims of success from methods that rest on neither a theoretical nor a clinical basis; these include removal of foci of infection, vaccines, dietary regulation (with the exception of reduction diets) and endocrine therapy. In spite of many claims to the contrary, critical evaluation of present evidence is entirely against an infectious, metabolic or endocrine etiology for degenerative joint disease.<sup>11</sup>

One of us (W. B.<sup>17</sup>) has stressed elsewhere the necessity for a careful distinction between degenerative joint disease and rheumatoid arthritis. Once the physician is sure of his ground, the first essential step is to explain the nature of the condition to the patient, thus dispelling the fear of crippling and disability that has undoubtedly arisen in the latter's mind and has been fostered by the comments of his associates. For this reason, it is better to avoid the use of the term, "arthritis," altogether, on account of its gloomy connotation and to stress the favorable prognosis possible for the preservation of function and the relief of pain.

In brief, the principles of treatment of degenerative joint disease consist in reassuring the patient and explaining to him the nature of the disease, correcting responsible factors, if present, and affording symptomatic relief, so far as possible. Since it is often impossible in a given case to separate symptomatic measures from those that have a more direct effect on the progress of the disease, no attempt will be made to do so in the following detailed consideration of treatment.

## METHODS OF TREATMENT

### *Correction of Contributing Factors*

Once the diagnosis of degenerative joint disease has been made and its nature and prognosis explained to the patient, the physician's next consideration should be to decide whether any irritating or accelerating factors can be removed or ameliorated. As a check, the previously listed contributing factors should be consulted. If occupational trauma is still going on, the patient may be advised to change or modify his job. Obesity obviously calls for weight reduction, which is dis-

discussed below. Foot strain and poor posture suggest the use of supporting plates, belts and corsets, and the strengthening of flabby muscles by exercise. The treatment of other static deformities usually requires orthopedic consultation. Intra-articular disease of a traumatic nature may demand surgery. If an infectious arthritis plays a causative role and is still active, specific treatment should be instituted at once.

### *Diet*

None of the special diets that have been loosely applied to various forms of chronic arthritis are indicated in degenerative joint disease.<sup>18</sup> Protein, whether or not in the form of red meat, need not be cut down on account of the joint symptoms. Carbohydrates should be limited only if necessary to reduce weight. Whether or not the diet is "rough" depends on the patient's needs in regard to intestinal activity, diverticulosis and so forth. So-called "acid fruits and vegetables" bear no known relation to the degenerative process. From the nature of the pathogenesis of the disease, as described above, it is difficult to see how diet can play a direct role. Many claims for the successful use of certain diets undoubtedly depend on the spontaneous subsidence of periosteal irritation from encroaching marginal osteophytes. In short, the only known value of dietary regulation in degenerative joint disease lies in the field of weight reduction.

We have mentioned above that obesity may be a precipitating or accelerating factor in degenerative joint disease. Conversely, weight reduction will often relieve symptoms to a striking degree. In markedly obese patients, the indications are obvious, but relief is often gained by the loss of 10 to 20 pounds in patients only slightly over weight. It is of advantage to have the patient lose the first 10 or 20 pounds rather rapidly so that he may be encouraged to persevere from both the evidence of the scales and his less painful joints. The most striking benefit from weight reduction is in degenerative joint disease of the knees, which occurs in overweight women at or about the time of the menopause.

### *Climate*

The symptoms of degenerative joint disease may frequently be brought out by exposure to dampness or cold. For this reason, it is wise to caution the patient against such exposure and to insist on warm clothing when necessary, including gloves for patients with Heberden's nodes and long underwear for those with knee involvement. If practicable for those living in northern latitudes, much discomfort and even exacerbations

may be avoided by migration to a warm, dry climate during the winter season.

### *Drug Therapy*

No specific drugs are known that will alter the course or permanently do away with the symptoms of degenerative joint disease. None of the recently introduced so-called "specifics" for the treatment of arthritis have proved efficacious when tested under controlled conditions; these include gold salts, sulfur and massive doses of vitamin D.

Analgesics are of real value, but should not be used to the avoidance of rest, correction of irritating factors and other measures of proved worth. Aspirin, in regular dosage of 10 gr (0.6 gm) every three or four hours, is effective and inexpensive. Five grains (0.3 gm) of phenacetin or  $\frac{1}{4}$  to  $\frac{1}{2}$  gr. (0.015 to 0.03 gm) of codeine may be added to each dose of aspirin, if necessary. Compounds containing amidopyrine or cinchophen had best be avoided owing to the possibility of rarely occurring but serious toxicity. If morphine is needed, the physician should be suspicious that some other serious condition is also present, notably metastatic cancer.

Potassium iodide has long enjoyed a favorable reputation in the treatment of degenerative joint disease, but in our experience no benefit has been derived from the use of this drug that could not be ascribed to other measures or to the natural course of the disease.

The use of small doses of thyroid is permissible to increase metabolism and thus aid in combating obesity, but no specific effect has been proved from the use of this drug or other endocrine preparations. Of course, if myxedema is present in a patient with degenerative joint disease, the symptoms may be aggravated. In such cases, the use of thyroid is indicated. Similarly, if the patient is a woman with menopausal symptoms, replacement therapy with estrogenic material may be helpful, but no direct effect on the joint disease can be expected.

### *Rest*

Hospitalization is rarely necessary for patients with degenerative joint disease. Diagnosis can usually be made in the office with the benefit of a careful anamnesis and examination, in addition to roentgenograms of representative joints and routine examination of the blood and urine, with the occasional aid of the blood sedimentation rate. In a few patients, symptoms due to traumatic synovitis with effusion are sufficiently acute to require hospital care. A few others, of course, require hospitalization because of necessary surgery. The majority of patients can benefit by



rest at home according to the directions of the physician, often without interfering with housewifely duties or means of livelihood. The prescription of rest should be definite and included in the written directions, which are of great advantage in the management of a patient with chronic joint disease. It is obvious that relief of strain to the weight-bearing joints, which are the usual sites of degenerative joint disease, can be gained by a sitting or preferably reclining position for certain intervals during the day. The amount of rest prescribed varies with the severity of symptoms and may be gauged by trial, the relief of pain being the criterion. A good start may often be made by getting the patient off his feet for a week or two, followed by rest periods for one or two hours during the day. If work must be carried out, the patient can rest in the noon hour and at home before the evening meal. Finally, the amount of rest prescribed must be tempered by two considerations. In the first place, the patient must not believe that he is a permanently crippled invalid, cut off from his usual occupations and hobbies. At every point, the rationale of treatment must be explained, and the relatively good prognosis emphasized. A second consideration is that, in common with other forms of articular disease, the joints tend to become stiff and painful if kept in one position too long.

In addition to rest for the patient as a whole, the involved joints may acquire protection from strain by the use of certain advantageous positions or mechanical supports. For the cervical spine, periods of rest in a supine position, with no pillow or a low one, are of benefit. For severer symptoms, a Thomas collar or head traction is necessary. Similarly, for involvement of the lumbar and sacroiliac articulations, the patient should lie on the back with the knees and hips flexed during rest periods. A hard mattress should be employed, and boards may be placed between mattress and spring. When the patient is up and about, strain to the spinal and sacroiliac joints may be avoided by a corset—a brace is rarely necessary. If the patient drives a car, he should be able to reach the pedals readily with the knees flexed; if necessary the seat should be moved forward or a pillow should be placed behind his back. Painful hips may be relieved for a time by rest in bed, with traction on the leg or the use of a spica of plaster or leather. Elastic bandages or, better, a laced, part-leather, part-elastic kneecap takes from the knees much of the stress and strain of walking. Crutches allow the patient to be ambulatory, yet take the strain off a painful hip or knee. If the feet are involved, usually only in the secondary type of degenerative

joint disease, support and correction of faulty mechanics can be gained by the use of heel lifts and footplates. The aid of the orthopedist can be sought with advantage in planning these measures for the care of individually involved joints.

### *Physical Therapy*

Symptomatic relief, one of the chief aims of therapy in degenerative joint disease, can be aided by physical therapy in the form of heat, massage and graded exercises. The mechanism of relief by the use of heat is thought to be increased blood flow, although there is no evidence that the circulation to joint tissue is impaired in this disease. Simple methods of providing heat to the joints are perfectly satisfactory and have the added advantage that they can be applied several times daily in the home. These methods include the use of hot packs, hot baths and an inexpensive electric-lamp baker. Diathermy and other electric machines using short-wave modalities for heating the deeper tissues are no more effective than the simple methods. The physician should give definite directions to the patient concerning the frequency and duration of treatments. In general, heat may be applied for periods of not over fifteen minutes, two or three times daily. A state of chronic passive congestion and tissue hypersensitivity can be induced by overenthusiastic baking. Gentle kneading or light stroking massage of the muscles surrounding affected joints can be applied following the administration of heat. Heavy massage or massage over the joint itself provides a harmful form of trauma, which may increase the patient's symptoms. It is therefore essential that the physician give exact directions for this method of treatment, whether it is administered by a member of the family or a trained physical therapist.

### *Exercise*

Exercise, like rest, can be divided into that of the patient as a whole and that of the involved joints. In general, although a moderate amount may be necessary for weight reduction, exercise should be prescribed with caution. The patient should be informed that in this disease of the joints, activity is not necessary to prevent ankylosis, and overexercise may bear a definite possibility of harm. Frequently, pursuit of the patient's usual occupation will be all that the joints can stand. Violent sports should be avoided, especially those involving maximal use of an affected joint. Postural exercises, which are important to relieve weight-bearing joints of unnecessary strain, should be increased gradually—never beyond the boundary of pain. The exercise program for

strengthening the muscles that control the affected joints is much more important than the use of heat or massage. So long as the joint is inflamed and the muscles that control it are fatigued, they should receive complete rest. When spasm and inflammation have subsided, carefully graded muscle-setting exercises are begun and are persisted in daily until satisfactory power has been regained.

### *Psychotherapy*

We have already alluded to the value of reassuring the patient and explaining to him the nature of degenerative joint disease. If freed from fear of crippling, the patient often bears with equanimity the occasional aches and pains that treatment fails to relieve. Other patients, especially those complaining of undue fatigability, have a lowered threshold of sensibility, which accentuates symptoms that might be borne without complaint by more stoical persons. In such cases, the lessening of domestic or business cares, vacations with change of scene, and the search for and eradication of disturbing elements in the environment are all important in securing a satisfactory therapeutic result. For these patients, regular doses of a mild sedative, such as  $\frac{1}{4}$  gr. (0.015 gm.) phenobarbital after meals and at bedtime, may be more helpful than the use of analgesics.

### *Special Types of Degenerative Joint Disease*

*Heberden's nodes.* Degenerative joint disease of the terminal joints of the fingers is probably the commonest type seen in general practice. Rheumatoid arthritis can usually be readily distinguished, even without the aid of x-ray study and sedimentation rate; one should bear in mind, of course, that the two diseases may be present in the same patient in an unrelated form. It must also be remembered that the process may spread to the proximal joints in 10 to 20 per cent of the cases, or even rarely begin there. Acute cases, with marked tenderness, pain and occasionally fluctuation, must not be confused with acute gouty arthritis or sepsis. This condition is commoner in women than in men, and usually appears around the age of fifty. Younger patients with Heberden's nodes often give a history of premature development of the nodes in other members of the family. There is no specific treatment for this benign form of degenerative joint disease. The patient is more comfortable if the hands are kept warm and if trauma to them is avoided. The important thing is to explain the situation to the patient, who usually fears the worst, and assure him that he is not going to develop a crippling

disease and that the nodes, if acute, will subside in the course of a few months, whether treated or not.

*Temporomandibular involvement.* As recently described by Costen,<sup>19</sup> a variety of symptoms may result from degenerative disease of the temporomandibular joint, caused by loss of molar support or by malocclusion. These complaints include otologic symptoms (deafness, tinnitus, pain, dizziness and nystagmus), headache (occipital and vertical), herpes of the external auditory canal and buccal mucosa, and burning or dryness of the mouth and tongue. Roentgenograms may show loss of substance of the head of the condyle anteriorly and of the articular eminence. The insertion of cork disks between the molars may give temporary relief and may serve as a therapeutic test. Permanent relief of symptoms belongs to the sphere of dentistry.

*Morbus coxae senilis.* The treatment of degenerative disease of the hip joint, morbus coxae senilis, calls for an individually designed program for each case.<sup>20</sup> If there is flexion-adduction deformity, a period of complete bed rest, with adhesive traction of the leg, may be necessary. Heat and massage, as described above, should be given daily. When the muscle spasm has subsided, carefully graded exercises for the hip abductors and extensors (the gluteus medius and maximus muscles) should be prescribed and followed over a prolonged period. Four to ten slow voluntary contractions or so called "sets" of each muscle group at one sitting are repeated two or three times daily unless there is evidence of strain or fatigue. Unilateral hip disease may be protected from the strain of weight bearing by crutches. In some cases, restriction of motion by means of a leather or elastic knitted hip spica gives great relief. If there is apparent shortening of the leg due to fixed adduction contracture, the heel of the shoe should be raised sufficiently to compensate for the apparent inequality of leg length.

This is the one form of degenerative joint disease that may lead to actual crippling in spite of the conservative measures described above. Orthopedic consultation is in order for such cases to determine the advisability and type of operation. In an occasional patient, reestablishment of proper weight bearing lines and improvement of function may be gained by osteotomy of the femur. In severe cases, help can be given by a plastic operation on the anterior wall of the acetabulum<sup>21</sup> or, better, by means of a vitallium-cup arthroplasty.<sup>22</sup> In the hands of the originator,<sup>21</sup> these operations have been extremely successful in relieving pain and increasing the range of joint motion in

severe, incapacitating cases. Such an operation can be applied equally well to young patients with degenerative changes secondary to a slipping femoral epiphysis, Legg-Perthes disease and intra-pelvic protrusion of the acetabulum.

### Surgery

There are few indications for surgery in the treatment of degenerative joint disease, except for those already mentioned. One is the removal of loose bodies or so-called "mice" from the knee joint if pain, locking or secondary inflammation is caused thereby. Conservative treatment should be given a trial, but if incapacitating symptoms persist and the loose bodies are demonstrable by examination or roentgenograms, removal should be carried out without delay, since the degenerative process may be hastened by their presence.

Acute traumatic effusions usually subside with rest and splinting; if they persist, aspiration should be done.

### PROPHYLAXIS

Measures to prevent the development of degenerative joint disease or the acceleration of its course, once present, should be obvious to the reader on consulting the list of contributing factors already given. Such measures fall properly into the field of preventive medicine, and constitute one of the responsibilities of both family physician and specialist. In handling fractures and sprains, diseases of the epiphysis, rickets, infantile paralysis and so forth, the physician must bear in mind the possibility of premature development of degenerative joint disease if the joints are left subject to unusual strain. Static deformities and postural defects should be corrected as speedily and as completely as possible. Obesity, especially in those approaching middle age, is hazardous to the well-being of the joints, as well as of the other bodily systems. Repeated joint trauma, whether occupa-

tional or recreational, should be advised against. Finally, in a patient with any form of arthritis, the possibility of secondary degenerative changes must always be kept in mind and guarded against, especially if the movements of weight-bearing joints tend to become limited in a position of mechanical strain.

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**CASE RECORDS OF THE  
MASSACHUSETTS GENERAL HOSPITAL**ANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor***CASE 27301****PRESENTATION OF CASE**

A thirty-seven-year-old housewife entered the hospital with the complaint of joint pains.

About eleven years before entry, the patient began having mild attacks of pain in the shoulders and hands, which recurred every spring and lasted about two weeks. These attacks were relieved by salicylates and applications of heat. Three years later, her tonsils were removed for this condition. The following year, she developed a painful swollen ankle, and the condition soon spread to most of her other joints. Since then, she had had intermittent joint pains varying in intensity from time to time and usually aggravated by cold weather. The pain was not severe enough to keep her from doing her housework. Three years before entry, she developed a cough, with substernal pain and fever but no chills. She entered another hospital, where she was found to have bilateral pleural effusions. The pleural cavities were tapped twelve to fifteen times, and she developed empyema on the right, which was drained for several weeks. For the next three years, the joint pains were severer, but the patient was able to do her housework. For a year before entry, she had slight dyspnea on exertion and edema of the ankles, which disappeared at night. Two months before entry, she had a sudden onset of nausea, vomiting and diarrhea, with some pain around the umbilicus. The pain was somewhat relieved by vomiting but made worse by defecation. She had twelve to fifteen bowel movements a day, which were said to contain mucus and blood. The diarrhea ceased after treatment with Fuller's earth, and the patient improved considerably. A few days later, six weeks before entry, she developed severe dysphagia, at first with solid foods and finally with liquids; she was unable to swallow anything because of the severe pain and vomited about once a day.

She re-entered the outside hospital, where she was found to be obviously ill, pale and somewhat emaciated. Her left chest was dull to flat posteriorly below the angle of the scapula, and distant bronchial breathing and egophony could be heard in this area. The heart was moderately enlarged

to the left, the rate was 120 and grossly irregular, and the sounds were of fair quality. No murmurs were heard. The blood pressure was 110 systolic, 60 diastolic. The abdomen was normal. An x-ray film of the chest showed fluid at the left base; the heart was displaced to the left. The blood showed a red-cell count of 3,470,000 with a hemoglobin of 65 per cent, and a white-cell count of 4000 with a normal smear. The blood Hinton reaction was negative, as were Widal and undulant-fever agglutination tests. A gastrointestinal series was negative except for "slight delay with slight narrowing at the extreme lower end of the esophagus, consistent with a mild degree of cardio-spasm." A nasal tube was inserted. The patient was given fluid through the tube for forty-eight hours, after which she was able to take fluids and soft solids by mouth. The irregular heart beat proved to be paroxysmal, the attacks lasting a few hours. Her temperature and respirations were normal. After ten weeks, she was discharged on a bland diet. One month later, she entered this hospital for study.

Physical examination revealed a somewhat undernourished woman with signs of fluid or of a high diaphragm on the left, and a heart enlarged to the left, with sounds of good quality and no murmurs. The abdomen was normal. There was slight to moderate pain on motion of the neck, back, elbows, shoulders and knees. There was swelling and tenderness of a few of the small joints of the hands.

The temperature was 98.6°F., the pulse 90, and the respirations 20.

Examination of the urine was negative. The blood showed a red-cell count of 3,780,000 with 65 per cent hemoglobin, and a white-cell count of 4300 with 86 per cent polymorphonuclears. The nonprotein nitrogen of the blood serum was 19 mg. and the fasting uric acid 4.7 mg. per 100 cc.; the sedimentation rate was 1.94 mm. per minute. The blood Hinton reaction was negative.

X-ray study showed moderate decalcification of the lumbar spine and hands. There was slight narrowing of the vertebral joints, and some surrounding soft-tissue thickening. The chest showed enlargement of the heart to the left, with a rather prominent pulmonary conus. There was marked thickening of the pleura along the right axillary line from the apex to the diaphragm, and a small collection of fluid at the left base partially obscured the diaphragm and the apex of the heart. There were small areas of calcification at both lung roots. The nasal sinuses were clear. An electrocardiogram showed low T<sub>1</sub> and T<sub>2</sub>, inverted T<sub>3</sub>, shallow T<sub>4</sub> and normal Q<sub>1</sub>.

The patient was given a transfusion and discharged somewhat improved.

Two and a half months after discharge, she developed an ulcer on the left external malleolus, which did not heal. She also developed over the spine several flat nodules that were the size of a ten-cent piece and lasted for several weeks. Eight months after discharge, she suddenly had a severe shaking chill, with pain in the right chest, which was aggravated by inspiration. She became nauseated and vomited, and had a headache, but no stiff neck or increase in joint pains. She developed a temperature of 104°F., the blood pressure dropped, and the pulse became relatively slow. She re-entered the outside hospital, where physical examination revealed an obviously very ill woman with slightly cyanotic lips and fingernails. The heart was enlarged to the left, the sounds were loud, and there was a systolic murmur at the apex, with a suggestion of a gallop rhythm over the mitral area. The blood pressure was 85 systolic, 50 diastolic. Percussion of the chest was normal, but in the right mid-back there were crackling rales and definite bronchial breathing. The abdomen was slightly distended, and the liver edge was palpable 5 cm. below the rib margin and quite tender. There was a small ulcer on the external malleolus surrounded by an area of erythema.

The temperature was 105°F, the pulse 100, and the respirations 20.

The urine contained the slightest possible trace of albumin and 10 to 12 white blood cells per high-power field and occasional granular casts in the sediment. The blood showed a red-cell count of 4,100,000 and a white-cell count of 22,000, with 86 per cent polymorphonuclears. The sputum contained pneumococci, but the blood culture showed no growth.

Two days after entry, the area of rales and bronchial breathing had increased in size, and x-ray examination showed an area of consolidation at the right lung root. The blood pressure had risen to 126 systolic, 80 diastolic. The following day, the patient was symptomatically somewhat improved, but her temperature remained elevated and definite dullness could be detected between the angle of the scapula and the spine on the right. There was apparently a small amount of fluid in the abdomen, and there was slight edema over the sacrum and about the hips. Her urinary output became markedly decreased, and intravenous Salyrgan had no apparent effect. On the eighth hospital day, the urine contained a large trace of albumin, with occasional red cells and 10 to 15 white cells per high-power field, but no casts. The nonprotein nitrogen of the blood

serum was 70 mg. per 100 cc., and the chloride was 88 milliequiv. per liter. The patient was given 1000 cc. of concentrated glucose and sodium chloride, but her urinary output remained low. Twitching of the muscles developed, and the breath became urinous. The edema of the back and abdomen increased, and numerous nodules, 0.5 to 1.0 cm. in diameter, could be felt in both supraclavicular areas. The temperature remained high, and the pulse and respirations became more rapid. On the tenth hospital day, her condition became definitely worse. She developed generalized convulsions and died. The total urinary output in the last four days was about 300 cc.

#### DIFFERENTIAL DIAGNOSIS

DR. ALFRED KRANES: It is difficult to know how to begin on this problem because there seem to be so many apparently unrelated and independent episodes. I think the simplest way is to discuss each one independently and try to fit them together, if possible, into some sort of coherent picture.

The illness apparently began when the patient was twenty-six, and joint pains occurred about once a year. The description of the pain at the onset is not diagnostic of any type of joint disease with which I am familiar, although as the disease progresses, rheumatoid arthritis seems to be more of a possibility than any other type of joint disease; however, one does not expect patients with that disease to have a recurrence lasting only two weeks and disappearing, leaving her perfectly well for the rest of the year.

Rheumatic fever is another unlikely possibility. The only type of joint disease that will recur and subside, permitting a patient to be well in between attacks, is gout, but there is very little in this story to make one consider that diagnosis very seriously. So that I think we shall have to leave unsettled the diagnosis of her joint disease for the time being and go on to the next episode, which is the development of bilateral pleural effusion three years before admission. One would like to know what type of fluid was removed from this patient's chest. That we are not told, since it was done elsewhere. I presume it was a serous effusion. One would also like to know over how long a period she was ill with these effusions, since she had twelve to fifteen taps. I should interpret the empyema as probably being the result of repeated taps and not part of the underlying disease. The effusions must have lasted at least several months to have been tapped as many times as recorded here. What produced the pleurisy is far from clear. The usual causes of pleural effusion do not seem to fit this picture. Tuberculosis, of

course, is the first thing one considers, but it is quite unusual to get bilateral tuberculous effusions. They do occur but not very commonly. Furthermore, it is extremely unusual for a tuberculous effusion to require tapping so often as this. Apparently, the fluid reaccumulated rapidly. I think the chief argument against tuberculosis is that the empyema cleared up in several weeks. I certainly do not believe a tuberculous empyema would clear up so rapidly. Other causes for effusion, such as cancer, do not seem to fit this picture very well. It would be unusual to have a bilateral effusion with a malignant neoplasm. The patient might have had lymphoma, but I think it is extremely unlikely. There seem to have been no signs or symptoms of cardiac failure or renal or liver disease. I shall therefore leave the question of the pleurisy unexplained for the while.

The patient then developed a totally new chain of symptoms—nausea, vomiting and bloody diarrhea. No details are given, and I doubt whether any satisfactory explanation for it will be found, since it did not recur. The chances are that what ever produced it had subsided at the time of death, and very likely no anatomic explanation may be forthcoming for these symptoms. The patient also developed severe dysphagia, which may also have been related to the lesion causing the previous abdominal symptoms. We can speculate about the presence of some ulcerative lesion in the mucous membranes of the gastrointestinal tract, but there is no direct evidence. The symptom cleared up, and nothing further is said about it.

The patient again entered the hospital with a left pleural effusion, which apparently was asymptomatic. No fluid was present on the right, since the right pleural cavity was probably obliterated by the previous empyema. This time, her heart was found to be enlarged, and she was apparently having paroxysmal fibrillation, although the exact nature of the arrhythmia is not described. The x-ray report disturbs me a bit, because it states that the heart was displaced to the left. If that is so, one must assume that there was collapse of a considerable part of the left lung. There is no apparent reason for it, and I wonder if that is a correct observation. Whether the heart was displaced to the left, we shall have to leave open to question, I rather doubt it.

The physical examination when the patient entered this hospital is more or less confirmatory of what was previously found, except that there appeared to be less fluid than was described before. Whether that was removed in the meantime or absorbed spontaneously, we are not told. Again,

the heart was found to be enlarged, and the rest of the physical examination was normal except for pain and swelling of the joints. The urine examination was negative, which is important since the patient died of renal failure, this is the only report we have of a urine examination during the whole illness. The secondary anemia and leukopenia are again confirmed, but the rest of the laboratory data are of no value except for an elevated sedimentation rate.

The electrocardiogram does not mean much to me except that the patient may have had some myocardial damage. Following her discharge, she developed an ulcer over the left malleolus, which persisted until her death some six or eight months later. There seems to be no adequate explanation for it. Nothing is said about varicose veins, and she apparently was not syphilitic. The nodules over her spine interest me, and I should like to know whether they were subcutaneous or in the skin, and whether or not the skin was discolored. The description here does not help one very much. The nodules disappeared, apparently, in several weeks. Then the terminal event occurred, which was quite obviously a pneumonia. The rest of the story is that of a patient dying in uremia. What the cause of this terminal renal failure is, one cannot say from the record. The first question that comes to mind in a patient with pneumonia is whether chemotherapy was employed. Was she given any sulfapyridine or sulfathiazole?

DR CHARLES L. SHORT: No.

DR KRANES: That is too bad; because I had a ready explanation for the terminal renal failure. We shall therefore have to look for other explanations. Patients with overwhelming acute infections occasionally die in uremia, as some post-operative patients do. The blood pressure drops, and the renal blood flow diminishes and is followed by oliguria, anuria and consequent uremia. That is possibly the explanation here. In addition, there may be some underlying diffuse disease of the kidney, which shut down terminally. It does not seem, however, like an ordinary acute glomerulonephritis.

The whole problem seems to resolve itself into whether this patient had a number of different diseases explaining these separate episodes, or whether one can tie them together under one diagnosis. It would be more logical to explain everything on one diagnosis in this particular case, because it seems to me that there are no satisfactory multiple diagnoses that could be made explaining these separate episodes individually. One would like to find a disease that would explain them all. It would have to be quite a widespread dis-

ease involving the small blood vessels of the body or some diffuse vascular lesion of which these episodes were local manifestations. So far as I can see, there are only two diseases that would adequately explain this picture. One is periarteritis nodosa. The other is disseminated lupus erythematosus. So far as I know the pains of periarteritis are much more likely to be muscular or neuritic, rather than articular, nor does the disease cause recurrent pleural effusions—I have never heard of its doing so, at any rate. Furthermore the laboratory evidence is against it. Patients with periarteritis nodosa usually have a leukocytosis and very often an eosinophilia, neither one of which was present in this particular case.

The diagnosis of disseminated lupus—"acute disseminated lupus" is a very poor term because one cannot readily speak of an acute disease that has apparently lasted eleven years—seems to fit this picture better than anything else. It explains to me practically everything this patient had. Joint pains are very common in that disease. Recurrent pleural effusions or involvement of any of the serous surfaces is an outstanding characteristic. The gastrointestinal symptoms can be explained on that basis because patients with disseminated lupus develop lesions of the mucous membranes. To be sure, the lesions are more likely to be in the mouth or pharynx, but they can occur in the lower gastrointestinal tract as well. It could also explain the cardiac symptoms, because it frequently involves the heart, especially the pericardium. We have no evidence of pericarditis here, however. Occasionally it involves the endocardium, producing atypical vegetations on the heart valves, and cases have been described in which the myocardium has been involved, although the pathology of the disease is not at all clear. The diagnosis of disseminated lupus would also explain the ulcer of the leg, since it occasionally produces ulcerative lesions on the skin. Finally, many of these patients die of uremia. It is well known that people with disseminated lupus may have very extensive renal involvement. It is also interesting to note that patients with this disease, very often up until the time of death, show no evidence of renal disease, and then with the advent of some acute infection develop uremia. On the whole, disseminated lupus explains the picture better than anything else.

But there are objections to it. The first is its duration. Rarely do people with disseminated or visceral lupus live this long. The second and more important objection is the fact that throughout the disease no mention is made of skin lesions, unless possibly the nodules described represented

involvement of the skin. One hesitates to make a diagnosis of lupus without skin lesions, but in the disseminated type, the cutaneous manifestations of the disease are the least important part. Since everything else fits so well, I cannot allow the absence of skin lesions to deter me from making that diagnosis, which has one other great advantage, namely, that there are no characteristic pathologic lesions. I think among pathologists there is quite a controversy about whether or not there are any characteristic lesions. The consensus seems to be that there are not. That being so, Dr. Mallory may find very little aside from the acute terminal pneumonia. Consequently, although we may not be able to prove the diagnosis, Dr. Mallory will not be able to disprove it.

DR. SHORT: I saw the patient on both admissions to this hospital, and four or five days before she died. At the time she was in this hospital, there were two diagnoses that we considered: one was Dr. Kranes's diagnosis of disseminated lupus, and the other was a form of rheumatoid arthritis, with pleural effusion, pericarditis and myocarditis. We had the same objections to lupus that Dr. Kranes had—the lack of any characteristic skin lesions. It is fair to say that she did have some small scattered papulopustular lesions, but we were never quite sure whether they meant anything or were just what one might see on anybody. The patient also had what seemed to be a mild acne rosacea; at least we thought it was, and did not consider it characteristic of lupus. The other objection was the duration of the disease—she had been ill for ten years, although she was in relatively good shape. When I saw her just before she died, I could add nothing more to a consideration of the primary diagnosis. I thought she had an intercurrent pneumonia and cardiac failure.

At the time I saw her here, there was no evidence of renal failure. I think it is fair to say that Dr. Walter Bauer and I both saw this patient, and that I leaned toward atypical rheumatoid arthritis and he toward acute disseminated lupus.

#### CLINICAL DIAGNOSES

Acute disseminated lupus erythematosus?  
Rheumatoid arthritis?  
Pneumonia.  
Terminal uremia.

#### DR. KRANES'S DIAGNOSES

Disseminated lupus erythematosus.  
Terminal pneumonia.  
Uremia.

## ANATOMICAL DIAGNOSES

Acute disseminated lupus erythematosus  
 Bronchopneumonia, bilateral  
 Miliary abscesses of right upper lobe of lungs  
 Pericarditis, chronic, fibrous, obliterative  
 Mediastinitis, chronic, fibrous.  
 Pleuritis, chronic, obliterative  
 Splenomegaly  
 Lymph node enlargement, general  
 Pulmonary congestion.  
 Arteriosclerosis, aortic, minimal  
 Peritonitis, chronic, fibrous, localized  
 Perisplenitis  
 Ascites

## PATHOLOGICAL DISCUSSION

DR TRACY B. MALLORY: The post mortem examination, as Dr. Krane predicted, still leaves several loopholes for doubt. The positive findings can be listed rather quickly. There was a complete fibrous obliterative pleuritis on both sides, with no fluid. The pericardium was quite markedly thickened, and Dr. Eugene Sullivan, who made the post-mortem examination, also thought that the surrounding mediastinal structures showed more fibrosis than usual. The pericardium was totally adherent to the heart, and the two together weighed about 500 gm. The right ventricle seemed to be slightly dilated and was definitely a little hypertrophied. There was no endocarditis, and no myocarditis was made out. The liver was enlarged, and showed rather marked central congestion, which merely seemed to be evidence of heart failure. The spleen was greatly enlarged, weighing 700 gm. It should have been readily palpable. The kidneys were also large, weighing a little over 400 gm. Through out the body, all the lymph nodes were quite notably enlarged, ranging from 0.5 to 1.5 cm in diameter. The retroperitoneal, bronchial, axillary and inguinal glands showed definite lymphadenopathy. The joints showed marked synovitis but no evidence of rheumatoid arthritis.

On microscopic examination, there is very little to add. There was a fibrous pericarditis, pleuritis, terminal pneumonia, some slight central necrosis of the liver and nothing significant about the spleen. The kidneys showed discouragingly little. An occasional glomerulus showed focal glomerulitis of a tuft, or of a portion of the tuft. They certainly did not look like the kidneys of renal failure and uremia. The convoluted tubules were a little swollen. Nowhere in the body were we able to pick up any vascular lesions that would suggest periarthritis.

We have the records of autopsies on 24 cases of disseminated lupus, and on reviewing them it is apparent that nothing is constant. Pneumonia is the commonest finding, but that is always just a terminal event and nonspecific in character. Pleuritis and pericarditis occur in the great majority of the cases. Ascites is less common, and endocarditis is uncommon. A diffuse lymphadenopathy is almost regular. Splenomegaly is quite typical. Nephritis, when one hunts very hard for minimal changes, can be found in 70 per cent of the cases. At the time of autopsy, the skin lesions could be made out in 14 cases. The existence of a real adhesive pericarditis, particularly a mediastinopericarditis, is unusual in these cases, but we have seen it and I should be strongly inclined to side with Dr. Krane and regard this case as one of disseminated lupus despite the absence of characteristic skin lesions at any time during the disease.

DR. KRANE: You have to make that diagnosis mostly on clinical grounds.

DR. MALLORY: Yes. We can add two more points that are consistent from the anatomic point of view: the slight changes in the kidney are of a type we see most frequently in lupus, and the changes in the lymph nodes are of the type we regularly see in lupus. Furthermore, the autopsy ruled out rheumatoid arthritis, tuberculosis and periarthritis nodosa, the only other likely possibilities in this patient.

## CASE 27302

## PRESENTATION OF CASE

*First Admission.* A forty seven year-old laborer entered the hospital complaining of hemoptysis.

At the age of twenty three years, the patient had had a penile chancre, and as a known syphilitic, he presented himself at the Out Patient Department seventeen months before admission for advice regarding the performance of manual labor. Fluoroscopy revealed a slight but definite enlargement of the heart in the region of the left ventricle, with a concave left upper border. The ascending aorta was prominent to the right, with increased pulsation; the hilar shadows and aortic knob were normal. On physical examination, the heart was regular at 80, with a moderately loud early diastolic murmur along the left sternal border. There was no Corrigan pulse, and the blood pressure was 205 systolic, 105 diastolic. Examination of the nervous system, as well as that of the pupils, fundi and fields, was negative. A blood Hinton reaction was positive, a lumbar puncture



normal, and the spinal-fluid Wassermann test negative. Antisyphilitic treatment was instituted, and the patient was allowed to do light work; he remained well without signs of heart failure, the blood pressure running between 205 and 140 systolic, 105 and 90 diastolic.

Six weeks before admission, the patient caught a cold in his chest, with a dry cough that finally produced small amounts of thick yellow sputum. On the day of admission, he suddenly began to cough up small amounts of bright-red blood every two or three minutes, so that at the time of observation he had raised about one and a half cupfuls. There were no accompanying symptoms and no pain.

In the hospital, there were no more hemoptyses, and on examination the patient appeared perfectly well. The fundi showed tortuous silverwire vessels, with dilatation of the veins at the points of crossing. There was a moderate pulsation of the neck vessels; the blood pressure was 180 systolic, 95 diastolic. Some confusion seemed to exist concerning the character and type of the heart murmurs. Systolic and diastolic murmurs were heard both at the apex and at the base by the various examiners in the Out Patient Department and in the hospital; however, the consensus leaned heavily toward the presence of a moderate systolic blow on the aortic area, with a moderate aortic diastolic murmur along the left sternal border. Scattered wheezes were heard throughout both lungs.

The temperature, pulse and respirations were normal.

The blood showed a red-cell count of 5,130,000 with a hemoglobin of 96 per cent, and a white-cell count of 9500. The blood Hinton reaction was positive. Examinations for tubercle bacilli in the sputum were negative.

An x-ray film of the chest showed no change, but on the fifth hospital day a line of increased density perpendicular to the diaphragm was present in the medial portion of the right lower-lung field, with a wedge-shaped area of consolidation close to it, apparently far posteriorly. No fluid was seen in the pleural cavity.

The patient's stay in the hospital was uneventful, and two weeks after admission x-ray study of the chest showed that the area of dullness had completely disappeared, so that he was discharged.

*Final Admission* (two years later). Although there was perhaps some slight decrease in exercise tolerance, the patient had felt well doing light work. Antisyphilitic treatment had been kept up in the Out Patient Department, but the blood Hinton reaction remained positive; the blood pressure ranged around 190 systolic, 100 diastolic.

Eight months before admission, an x-ray film of the chest showed that the heart had increased slightly in size since the previous examination, the enlargement being in the left ventricle. The aorta had become slightly wider and showed a Corrigan type of pulsation.

In recent months, a to-and-fro murmur over the aortic area and down the left border of the sternum was noted frequently in the Out Patient Department, as well as an apical diastolic blow.

Three hours before admission, after a meal, the patient was seized with a sudden, severe, non-radiating substernal pain, which was constant and still present on admission. Nausea and vomiting soon followed, with rapid cyanosis and cold, clammy extremities.

On examination, the patient was well developed and well nourished, orthopneic, cyanotic, cold, clammy and sweating. The eyeballs were roaming, the pupils equal. The heart was enlarged, the apex being in the anterior axillary line. The sounds were of fair quality, with occasional extrasystoles and a diastolic murmur along the left sternal border. The pulse was barely obtainable, the rate 90, and the blood pressure 60 systolic, 0 diastolic. The lungs were clear, and the respiratory rate was 25. The abdomen was normal, and there was no peripheral edema.

An electrocardiogram showed a normal rhythm, with a rate of 90 and a PR interval of 0.15 second. There was a depressed take-off in ST<sub>1</sub> and ST<sub>2</sub>, with prominent T<sub>1</sub> and T<sub>2</sub>. T<sub>3</sub> was upright, and R<sub>4</sub> low, with a depressed take-off in ST<sub>4</sub>.

The patient died eight hours after admission, without change in his physical signs.

#### DIFFERENTIAL DIAGNOSIS

DR. EDWARD F. BLAND: As a background for this patient's acute and rapidly fatal illness, I think there can be no reasonable doubt that he had a variable but considerable degree of hypertension and enlargement of the heart, which I am inclined to attribute mostly to the hypertension, rather than to the aortic regurgitation that was also present. The degree of aortic regurgitation seems not to have been great, certainly as judged by the blood-pressure (pulse-pressure) readings taken from time to time. Secondly, there apparently was no doubt in the minds of those who had this patient under their care that he also had cardiovascular syphilis, and I agree with that impression because he had a history of a penile lesion some twenty years before admission, a positive blood Hinton reaction, an aortic diastolic murmur, and fluoroscopically a slightly dilated ascending aorta, with increased pulsations. Although there was some confusion about the murmurs, I

think we had better rely on the interpretation of the majority, and accept the aortic diastolic murmur as diagnostic of organic aortic regurgitation, perhaps of only slight to moderate degree. The syphilis was vigorously treated.

I wonder if we might look at the X ray films and ask the X ray Department if they agree that syphilitic aortitis was present.

DR JAMES R. LINGLEY: This is the first film taken, showing enlargement of the left border, which was due to left ventricular enlargement. The aorta is tortuous, and there is some bulging of the anterior portion of the ascending aorta, but the dilatation is very slight. I think that from the X ray appearance it could be simply due to hypertension, and does not necessarily indicate syphilitic aortitis. This was the area of density described in the mid portion of the right lower lobe—rather a hazy indefinite area extending in a wedge posteriorly into the chest wall.

DR BLAND: Was that film taken two years before the final illness?

DR LINGLEY: Yes.

DR BLAND: Dr Aubrey O. Hampton and others make the point that calcium in the ascending portion and not visible elsewhere in the aorta is strongly suggestive of syphilitic scarring. Do you see any evidence of that?

DR LINGLEY: No. I see no evidence of calcium in the first portion of the aorta. These are later films, showing possibly a little more prominence in the region of the left ventricle, the aorta may be slightly larger, but I think it is rather doubtful.

DR BLAND: There is certainly no sacular aneurysm.

DR LINGLEY: No.

DR BLAND: There is no calcified aortic valve that you can see?

DR LINGLEY: No.

DR BLAND: Although the X ray films are not so helpful as I had anticipated, I think this patient probably had cardiovascular syphilis, with syphilitic aortitis; this was well treated, and the course suggests that this condition was not actually progressive. He got along very well, and there was not much evidence, either from symptoms, from signs or from interval X ray study, of a progression in the cardiovascular syphilis. On the first admission to the hospital, two years before he died, he had had a respiratory infection prior to entry. He was raising some blood, and developed what looks to me from the X ray description more like an infarct of the lung than pneumonia. I think this episode probably had no bearing on the later terminal acute illness.

Now we come to the last illness, the patient having had no angina, no paroxysmal dyspnea and no other cardiac symptoms in the interim. Patients with cardiovascular syphilis are notoriously apt to die suddenly either with or without preceding cardiovascular symptoms. It is difficult at first glance not to connect the two in this patient. Some die suddenly from rupture of a large sacular syphilitic aneurysm, which this patient did not have. Others die of acute coronary insufficiency, usually associated with free aortic regurgitation, indicating that the process has extended to a considerable degree about and beyond the mouths of the coronary arteries. Most of these patients, however, have some indication of acute coronary insufficiency before the sudden exitus. I do not believe this patient had free aortic regurgitation, and hence he probably did not have extensive narrowing of the coronary ostia. We can conceive that the coronary arteries were abnormally high in the aorta at their origin and perhaps being extensively involved without much indication of involvement of the aortic valve as such. I think that, however, is unnecessarily fanciful and needs no further consideration here.

How else, then, could cardiovascular syphilis suddenly cause this patient's death? It is well known that patients with syphilis may die abruptly and unexpectedly after specific intravenous treatment. This patient had been under treatment for some time without suspicious reactions, and nothing is said of very recent antisyphilitic therapy, so that I think we must assume his death was not related to therapy. In view of the foregoing remarks and with some hesitation, I shall say that I think cardiovascular syphilis had no direct bearing on his death.

What else might he have had? One must consider, at least in passing, a massive pulmonary embolus. When anyone dies in this fashion with severe pain in the chest, one has to keep that in mind. Furthermore, this man had probably had a small pulmonary infarct two years before, but I do not see that we have any reasonable evidence to attribute his death to a large pulmonary embolus. He had not been in bed. There was no infection, no obvious circulatory stasis, no swelling of the legs to indicate local vascular disease, and his veins were not engorged prior to exitus. Therefore, I am willing to discard pulmonary embolism from further consideration.

We are left with the two conditions, one of which seems to me most likely to have caused his death. First, and on the line of chances most likely, is a coronary thrombosis (myocardial infarct). The patient may certainly have had an

acute coronary thrombosis. One can work up a good case either for or against that diagnosis. Somewhat against it was the absence of preceding angina pectoris. Of course, that is not necessary. Secondly, it is a little unusual to have such severe pain as this man had beginning so abruptly; in fact, as described it was maximal at the onset. The discomfort with coronary thrombosis usually begins, as the patient often describes it, as "indigestion," which progressively increases in severity. In a few minutes to an hour or two, it becomes severe, but it is usually not maximal right from the beginning. Perhaps the description here is faulty, and I am too much disturbed by the abrupt onset. Perhaps it did start, after all, with less severe intensity and build up. However, I find other points that influence me somewhat away from this diagnosis. Ordinarily, with coronary thrombosis and myocardial infarction sufficiently extensive to end fatally in a few hours and with pain of this severity, it generally spreads somewhere else, usually to the arms, to the throat or to the back. I am bothered a little by the fact that this severe pain, if of coronary origin, remained so localized. Another point, — I am arguing against coronary thrombosis, and I think arguing myself into a hole, — the electrocardiogram is rather non-committal. It was probably taken in the Emergency Ward, because the record is obviously from a portable machine. As stated in the record, it is surprisingly close to normal and certainly not what one would expect if one were dealing with coronary thrombosis. There is a very slight depression of ST<sub>1</sub> and ST<sub>2</sub>, and no elevation of the ST interval in any lead. These are, at most, minor changes, and besides we do not know that this patient may not have been on digitalis prior to entry. Certainly, one cannot support a diagnosis with this electrocardiogram. The pulse rate was quite slow, in the absence of block, for a patient with a large myocardial infarct: it was only 90, and the degree of peripheral collapse was extreme. The drop in blood pressure, however, fits in beautifully with coronary thrombosis.

The next possibility, of course, is dissecting aneurysm. The abruptness and severity of the pain at the beginning is influencing me considerably in the latter direction. Usually, with dissecting aneurysm, the pain does not radiate to the arms, unless one of the vessels to the extremity becomes obstructed at its mouth. It often does go to the back and down into the abdomen, and even to the legs. In this patient, the pain *did not* radiate at all, and the blood pressure dropped rather alarmingly. Both are somewhat against dissecting aneurysm, but do not rule it out. The low pressure might be due to local disturbance of the vessels.

But that is forcing the point a little. The patient continued in a critical condition and died about eleven hours after the onset. The strongest argument against dissecting aneurysm is that we believe this patient had syphilitic aortitis, and the combination is certainly most unusual. I cannot think of any other argument either for or against these two most likely possibilities, and I prefer the latter.

In closing, I suggest as the diagnoses: hypertension and hypertensive heart disease, cardiovascular syphilis (not extensive), aortic regurgitation (slight) and dissecting aneurysm of the aorta. I prefer the latter to coronary thrombosis.

DR. WILLIAM B. BREED: Would Dr. Lingley have talked very much about the aorta or aortitis if he did not know that the patient had a positive blood Hinton reaction and had been treated for syphilis?

DR. LINGLEY: No. The only thing from the x-ray point of view that suggests aortitis is the fluoroscopic note of increased pulsations. From the films alone, I could not make a diagnosis of syphilitic aortitis.

DR. BREED: Do you think the pulse rate of 90 is a fairly good argument against occlusion?

DR. BLAND: No; it is no argument either way. Do you not think that most people who have myocardial infarction of this degree, and who fail and die in the course of twelve hours, show some signs of heart failure either by a gallop rhythm or by rales at the lung bases?

DR. BREED: I do not know that that is a good enough argument.

DR. WYMAN RICHARDSON: I should like to ask whether most patients with dissecting aneurysm do not have an even higher blood pressure than this. It has been my experience that most of them have systolic pressures over 200.

DR. BLAND: Most of them do, but not all. Some are under 200. This patient's age does not help us either way. Of course, one can get dissection on bases other than media necrosis cystica. Dr. George M. Bartol, of the Boston City Hospital, recently demonstrated at a meeting of the New England Heart Association the case of a seventy-five-year-old man with calcific disease of the aortic valve and superimposed subacute bacterial endocarditis. This man developed between two cusps of the aortic valve a mycotic aneurysm that broke through into the middle coat of the aorta and dissected widely. There was no evidence in this case of cystic degeneration of the media.

DR. BENJAMIN CASTLEMAN: But there was an infectious process.

DR. BLAND: Yes; but does it not illustrate that,

very rarely, degeneration of the media is not necessary to make possible a widespread dissection?

DR. CASTLEMAN. Years ago, it was believed that arteriosclerosis per se was the etiologic agent. The intima was arteriosclerotic, and the tear in the media occurred at the site of the arteriosclerotic plaque. We have had seven or eight such cases, but in those the dissection was limited to a short segment, not more than a centimeter or two, and did not produce any symptoms—just incidental autopsy findings.

DR. BLAND: Do you like the abruptness and severity of the onset in this case, Dr. Breed, in relation to your diagnosis of coronary disease?

DR. BREED: That does not bother me.

#### CLINICAL DIAGNOSES

Coronary thrombosis.

Syphilitic and hypertensive heart disease

Syphilitic aortitis and aortic regurgitation

#### DR. BLAND'S DIAGNOSES

Hypertension and hypertensive heart disease.

Cardiovascular syphilis

Aortic regurgitation, slight.

Dissecting aneurysm of the aorta.

#### ANATOMICAL DIAGNOSES

Dissecting aneurysm of aorta, with rupture into pericardium.

Media necrosis aortica cystica.

Syphilitic aortitis.

Cardiac hypertrophy.

Endocarditis, chronic, rheumatic, with stenosis, aortic.

#### PATHOLOGICAL DISCUSSION

DR. CASTLEMAN. The autopsy showed an enlarged heart, weighing 700 gm., and slight coronary disease without occlusion. The aortic valve showed definite interadherence of the cusps at their commissures, a finding quite characteristic of old rheumatic infection. There was no evidence of separa-

tion of the cusps to suggest syphilis. On the other hand, the aorta above the valve in the ascending portion and in the arch showed stellate scarring and linear tree barking characteristic of syphilis. This was confirmed microscopically. The ascending aorta was dilated, and measured 11.5 cm. in circumference. About 2 cm. above the aortic valve was a transverse tear in the intima. The tear was the largest we have ever seen, measuring 8 cm. across. Extending backward from the tear was characteristic dissection of the media of the aorta as far as the annulus, producing constriction of both coronary arteries, a circumstance that may cause anginal pain. As a matter of fact, the dissection must have continued into the coronary arteries because grossly there were subendocardial myocardial hemorrhages, and on microscopic examination there was adventitial hemorrhage around a few of the smaller myocardial vessels. Perhaps this was merely adventitial expansion of the blood around the coronary arteries. The dissection had not ascended above the point of intimal tear, stopping short at the point where the syphilitic aortitis became evident. The external tear had occurred into the pericardial cavity, and the patient presumably died of cardiac tamponade. As in another case we have recently discussed, there was hemorrhagic extension through the adventitia of the aorta to the adventitia of the main pulmonary artery and then into the lung. In summary, therefore, this man had rheumatic heart disease with aortic stenosis and probably some degree of regurgitation, syphilitic aortitis and a dissecting aneurysm of the aorta, with rupture. Sections of the aorta showed in addition to the syphilis a diffuse mucoid degeneration of the media, and in a few areas there were suggestive cyst formations. The cause of the dissecting aneurysm was most certainly the medial necrosis, and the syphilis was probably only an incidental finding. It is quite possible that the syphilitic scarring prevented the distal extension of the dissection.

DR. BLAND: Was the mitral valve all right?

DR. CASTLEMAN: Yes.

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## ANNUAL MEETING OF THE AMERICAN MEDICAL ASSOCIATION

THE annual meeting of the American Medical Association taxed the capacity of the hotels at Cleveland and even filled to overflowing a large lake steamer moored at the docks. It should be noted that the House of Delegates finds it an increasingly difficult problem to select cities capable of handling this tremendous gathering of physicians—hotel accommodations must be adequate, and at the same time, sufficient meeting places must be available for the House of Delegates, the various sections and the scientific and commercial exhibits. In spite of the crowding, the meeting was an outstanding success. The scientific exhibits were remarkable in their completeness and ar-

range, and the papers were up to their usual standard of excellence. The Cleveland Public Auditorium proved adequate for the meetings of the sections and for the exhibits.

The general atmosphere of the House of Delegates was saturated with preparedness, approached from military, social and economic angles. President Nathan B. Van Etten, in his address to the House, again urged a department of health at Washington, headed by an officer of Cabinet rank, a suggestion that, up to the moment, has received but little sympathy in Washington. President-elect Frank H. Lahey stressed the necessity of subordinating all trivialities and conflicts of opinion to the pressing need of national unity and preparedness.

The Committee on Preparedness, appointed at the meeting in New York City last year, presented through its chairman, Dr. Irvin Abell, a lengthy report detailing its activities. This report is presented in full in the June 21 issue of the *Journal of the American Medical Association* and should be read carefully by all physicians. It stressed particularly the deferment of medical students and interns by local draft boards, so that a constant supply of well-qualified physicians should continue. On recommendation of this committee, the House later adopted a statement to be sent to the Secretary of War and the Surgeon General of the Army urging the War Department to provide some form of military status for all students in approved medical schools and for all premedical students accepted for enrollment in approved medical schools, to make clear that in preparing themselves to become physicians such men are not trying to evade their responsibilities or the draft.

The Committee also recommended, and the House adopted, a resolution urging the creation by the Government of a central authority for the procurement of physicians for assignment to the United States Army, Navy and Public Health Service and to the civilian and industrial needs of the country. This agency would contain in its membership representatives from the civilian medical profession, and would have authority to determine who should be called to service and

who should stay at home. Although the Committee on Preparedness has the machinery to prepare lists of available physicians and is able to evaluate their capabilities and, in some measure, their necessity at home, it has no power to enforce its judgment; neither has the Government at the present time. This authority would have some power, and should function so that whole communities would not be left without adequate medical care.

A certain amount of unrest among many physicians in regard to the various specialty boards was brought into the open by two resolutions presented to the House. The first proposed a committee from the House of Delegates to confer with the various boards, and the second that efforts be directed toward creating a board of general practitioners. Neither resolution prevailed. It was the consensus of the delegates that the boards were independent of the American Medical Association, being more or less controlled by the Advisory Board for Medical Specialties.

The House of Delegates, in executive session, listened to a résumé of the trial of the American Medical Association and certain of its constituent societies in Washington and voted, without a dissenting vote, to authorize the Trustees to appeal the verdict to the Court of Appeals of the District of Columbia and, if necessary, to the Supreme Court of the United States, so that it shall once and for all be determined whether medicine is a trade or a profession.

A significant feature was the designating of the 1942 meeting at Atlantic City as the Pan American Session, to which the South American medical societies will be asked to send special representatives.

The free and open discussion, the careful thought given by the reference committees to each resolution and the high percentage of attendance at the meeting speak well for the quality of men selected by the constituent state societies as delegates to the House of Delegates. This is as it should be, since the House of Delegates is the only body that has the power to determine the policies of the American Medical Association.

## THE EPIDEMIOLOGY OF CANCER

ALTHOUGH, in its narrower interpretation, the term epidemiology can hardly be applied to a non-infectious disease such as cancer, nonetheless the methods applicable to the study and control of epidemic diseases are so serviceable in advancing the knowledge of cancer and its control that the utilization of the term in this broader sense is perhaps justifiable. The epidemiologist deals with disease processes in mass and is concerned not so much with the problems of the care of the patient as with learning all he can regarding the etiology, predisposing factors, nature and prevalence of the sickness. With these in mind, means of prevention and means of control may, at least to a limited degree, be worked out.

The first problem to be settled with regard to cancer is that of its incidence. Work has been done in this field for many years, and modern mortality statistics are fairly accurate. But even yet there is very little useful information regarding the morbidity of cancer. As more and more cases are cured, and as the different types of the disease have means of therapy developed for them, it becomes of increasing importance to know as many as possible of the details of incidence. In several localities, morbidity studies are now being carried out, and it is hoped that much may be learned from them.

The increasing accuracy of mortality statistics and the mass of data accumulated in hospitals have already demonstrated many things about cancer. Although it was once considered a disease of old age, it is recognized that certain types occur early in life, and some, such as tumors originating from nerve cells, are almost entirely restricted to that period. In general, it is true that the prevalence of cancer rapidly increases with the advance in years. Sometimes a given type of cancer, such as osteogenic sarcoma arising in bone, may have two different peaks of incidence in relation to age—one in adolescence and the other in old age. The occurrence of this tumor in old age is clearly correlated with a predisposing condition—Paget's disease in the bone. From these few examples, it may be seen that cancer is not one disease, but

rather many diseases different in their courses, in their modes of treatment and, presumably, in their causation.

Some years ago it was noted that workers in certain of the aniline-dye industries developed cancer of the bladder with unusual frequency. By careful observation of these cases, and comparison of the incidence of bladder cancer with that of the general population and with that of workers in other portions of the industry, it was finally found that one particular substance—naphthylamine—was the responsible factor, and that by preventing exposure to it this particular hazard could be overcome.

Still another example of special causation of a particular type of cancer is afforded by a group of miners at Schneeberg, in Austria, who worked in a mine where the ore was radioactive; because of the inhalation of radioactive particles over a period of years, many of these men developed cancer of the lung. Furthermore, the early workers in x-ray and radium provided excellent, though unfortunate, examples of the potential danger of these useful diagnostic and therapeutic tools, since the toll of skin cancer among this group of workers was exceptionally high.

In the past year or two, it has begun to be realized that an industrial hazard only recently thought to be fairly clearly understood might also produce neoplastic disease. The production of severe anemia by benzol poisoning has been known and recognized for some time, but the fact that with slight exposures a hyperplastic response of the marrow, leading to the development of leukemia, might occur has only recently been appreciated.

Race is a significant factor, but one difficult to evaluate, since many aspects of environment, habit and diet may be associated with it. The rarity of cancer of the cervix in Jewish women and the frequency of carcinoma of the stomach among Scandinavian races are examples of this type of race selectivity. Still another complicating factor in an understanding of the incidence of malignant disease is the existence of individual susceptibility. It has been clearly demonstrated that the occurrence and cure of one cancer con-

fer no immunity, but rather that there is a definite susceptibility of a person who has one cancer to the development of a second, or even of a third. These matters of racial and individual susceptibility are most troublesome when it comes to evaluating statistical material.

Certain lesions, some inherited and some acquired, are clearly recognized as precancerous. Thus, the occurrence of benign polypoid growths of the large intestine is an inherited abnormality, and such growths are a very frequent source of cancer of the large intestine. In the same way, certain acquired abnormalities subsequently lead to the development of cancer. Thus, there is a greater proportion of skin cancer in the total of all cancer in the South and Southwest than there is in New England, apparently directly ascribable to a greater exposure to sunlight, heat and dust. The woman who develops cystic disease of the breast develops a precancerous lesion. This type of disease process, quite prevalent, has been regarded by some as harmless, by others as a definite precursor to cancer. Only recently has a clear-cut answer to this problem been reached. On the basis of a large number of women followed for an average of over nine years, it was found that those women who developed chronic mastitis before the menopause had eleven and a half times as much cancer of the breast as the normal population did; after the menopause the difference was less striking—two and a half times as much. Furthermore, it is practically axiomatic that a cancer never develops in a normal mouth. Instead, one finds as predisposing factors such changes as leukoplakia, syphilis of the tongue and chronic irritation from bad teeth.

Progress will continue, if, as one learns more regarding the varied aspects of cancer, the disease is studied by epidemiologic methods, rather than by considering each case as an isolated problem. Means of prevention of certain types of cancer are already available. Methods of therapy are steadily improving, and their early application will lead, even without further advances in knowledge, to a marked lowering of the cancer death rate.

## MEDICAL EPONYM

## JACKSONIAN EPILEPSY

This condition bears the name of John Hughlings Jackson (1834-1911). The following quotation was written by an anonymous contributor to the column, "Reports of Medical and Surgical Practice in the Hospitals of Great Britain," and appeared in the *British Medical Journal* (1: 773, 1875) under the title, "London Hospital: Clinical memoranda of a series of interesting cases of nerve disorder now in hospital (under the care of Dr Hughlings Jackson). . . ."

... In the convulsions spoken of (commonly called epileptiform convulsions), a good deal occurs before the patient loses consciousness. One patient gave a very vivid account of what Dr Hughlings Jackson calls the "march of the spasm." This patient's fit begins in his left index finger and thumb, it then passes up the arm, and affects the face, and next passes down the leg. It is the rule that fits which begin in the hand should begin in the index finger and thumb when they begin in the foot, they usually begin in the great toe.

Speaking of these cases, and with reference to their difference from such cases as are commonly called epilepsy par excellence, Dr Hughlings Jackson said that he thought the abrupt division into cases with and cases without loss of consciousness was not even justifiable on grounds of convenience. The distinction was, he insisted, into cases where consciousness was lost first of all, very early or late in the paroxysm.

R W B

## MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS  
AND GYNECOLOGY\*DEATH ASSOCIATED WITH PERITONITIS  
FOLLOWING CESAREAN SECTION

A thirty seven year-old para VII had consulted no physician until labor started. Shortly after the onset of labor, the patient began to bleed from the vagina and was sent into the hospital. The membranes ruptured shortly after arrival in the hospital, at 6 35 p.m., and labor ceased. The hospital notes state that there was a good deal of bleeding during the night, and that at 3 30 the following morning a consultation was held. No diagnosis was made, and a cesarean section was performed. The pulse at that time ranged from 140 to 150. When the abdomen was opened, the baby and the placenta were found free in the abdominal

cavity. The uterus had apparently contracted, and there was no evidence in the note that the uterus had ruptured. The diagnosis of the operator was abdominal pregnancy, and the abdomen was closed. The patient was not transfused. She died three days after operation, apparently of peritonitis.

*Comment.* The record on this case is very incomplete. The past history mentioned only that she had had no evidence of cardiac or renal disease. The blood pressure was not recorded, and the only reference to the pulse was that before operation it had risen to 150. Although the death certificate attributes this death to abdominal pregnancy, such a diagnosis is extremely unlikely. Abdominal pregnancies are not characterized by excessive vaginal hemorrhage. The large amount of external bleeding in this case suggests that the placenta had been attached to the uterus, and the fact that the baby and placenta were reported to have been found free in the abdominal cavity, the placenta being without any attachment, bears out this diagnosis.

The observation that shortly after 6 35 p.m. labor ceased but hemorrhage continued is interesting. It is perfectly possible that, when labor ceased, rupture of the uterus occurred. Uteri do spontaneously rupture at term. An operation, followed by transfusion, when this patient arrived, after an intelligent diagnosis had been made, would probably have saved her life. To avoid such disasters, patients must be followed during pregnancy. Those financially unable to have private physicians must be taken care of by some sort of clinic. Without prenatal care, there can be no personal relation between patient and obstetrician, which is a vital part of successful obstetrics. It is difficult to understand how this patient, who was reported to have been bleeding very freely by vagina at 6 35 p.m. and who continued to bleed for nine hours, passing clots, had no vaginal examinations during this time for the purpose of establishing an intelligent diagnosis. Had an abdominal pregnancy existed, which is unlikely, and had it been diagnosed at 6 35 p.m., an operation at this time would probably have saved the patient's life.

This death can be attributed to either ignorance or indifference on the part of the medical attendant. A higher sense of responsibility throughout the profession at large can be acquired only by improved education in medical schools, by additional training in a hospital after graduation and by a greater sense of responsibility on the part of the hospital authorities so that they will demand of those physicians practicing in their institutions

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, Secretary, 339 Dartmouth Street, Boston.



a higher standard of obstetric routine. In this column, it has frequently been emphasized that hospital trustees are ultimately responsible for both good and bad medicine, and good and bad obstetrics, as practiced in their institutions. They have the power to regulate obstetrics in their hospitals, and until supervised obstetrics is practiced in all institutions, such fatalities as this will be repeated.

### INFANTILE PARALYSIS\*

Almost every summer, when infantile paralysis breaks out in some section of the country, there is an extraordinary degree of apprehension. This is not so much because of the large number of cases, as compared with epidemics of other diseases, but because of the fear of paralysis. Then, too, the unexpectedness with which the disease strikes and the uncertainty as to where it will appear add to the alarm. This feeling of helplessness is responsible for a pressing demand for more knowledge about the disease. As a result, infantile paralysis has been studied much more closely than many of the far commoner diseases to which we seem to have become more accustomed.

In many diseases, the cause is quite apparent from some striking circumstance; for example, the connection with the sick parrot in psittacosis and with the dog-bite in rabies and the exposure to a case in smallpox or measles or to the carrier in typhoid fever. But in infantile paralysis, no one circumstance immediately tells us which way to turn in attacking the problem. Any theory becomes a subject of study. Through the years, a great variety of seemingly contradictory findings have accumulated. Moreover, the clinical disease is sparsely distributed, and the available tools to study it in the laboratory are so restricted that studies in the field or experiments in the laboratory have often been limited to such small numbers that it has been difficult quickly to recognize the important or to rule out the unsound theories. Since it is difficult to discriminate between significant and insignificant observations, it is not easy to harmonize the various findings into a convincing concept. The result has been that we find all sorts of conflicting hypotheses, often based on small bits of evidence, and with seeming preference for those that have a more hopeful sound or match in oddness the vagaries of the paralytic disease. If, instead of forming a new theory every time a new bit of evidence is collected, the many pieces of evidence are fitted together like the jigsaw puzzle, we can begin to see a picture that could hardly be imagined from even the closest examination of the pieces separately. From the maze of collected studies, a few facts stand out clearly, facts that could not be discovered from the study of individual cases or epidemics, or from any single experiment.

The dissemination of the virus far exceeds the occurrence of the frank disease. Evidence that the virus is generally and rather uniformly widespread is seen in the geographic prevalence of the disease—we find it all over the globe; in the difference in the ages at which it occurs in city and country populations; and the finding

that many persons become immunized who have never had any symptoms of the disease. In striking contrast, the occurrence of the paralytic disease is restricted to a small fraction of those exposed to the virus.

Many who come in contact with the virus show no symptoms. More of the milder forms of the disease are now being recognized, so that a diagnosis of infantile paralysis no longer means, as it did a few years ago, inevitable paralysis. And we are beginning to ask ourselves when we see these primary symptoms: Will this be infantile paralysis, or is it merely a harmless infection with its virus, trivial in itself, but taking its full part in passing the virus along and keeping it in circulation?

Now that we understand that this virus, which is so widespread,—perhaps as widespread as measles,—is harmless to the vast majority of people, we might do well not to concentrate all our efforts toward the probably impossible task of keeping it from spreading, but rather to study the circumstances that, in addition to exposure to the virus, make for the occurrence of paralysis in the exceptional few of those exposed. There are reasons for believing that a difference in those exposed, rather than any difference in exposure, determines whether or not paralysis occurs. Paralysis picks not just any who are exposed, but a certain few. Some of these selectivities may give a clue of the cause of this susceptibility to paralysis, and this appears to be one of the most important things to learn about the disease, because paralysis is the one serious consequence of infection with this virus.

What are the selections that govern paralysis? The frequency of paralysis in those exposed varies in different climates, and also with season in the same locality. There are many persons who are exposed without having the recognizable disease in regions nearer the equator, and this is also true in off-seasons in temperate zones, where infantile paralysis is commoner. This influence of climate and season on the prevalence of the disease suggests that some physiologic process, which fluctuates with climate and season, conditions the response of persons to exposure to the virus.

A reason for believing that some factor in the patient determines the development of the disease on exposure to the virus is its tendency to occur in multiple numbers in some families, not only in brothers and sisters, but in members of successive generations, and in both lineal and collateral lines. This familial frequency is out of proportion to the low incidence of the disease in the general population, and suggests that susceptibility is in some way associated with an inherited quality.

That the disease tends to occur in persons of a certain constitutional type has long been suspected by those who see many cases. The observation, although by no means universal, has nonetheless been made often enough to suggest that children, whose glandular functions regulating growth and development are in some way modified, are more susceptible to paralysis than others.

Again, the virus of infantile paralysis evidently enters the system through the mucous membrane of the upper respiratory tract, and this mucous membrane, when sound, is probably the barrier that prevents the virus from reaching the nervous system. A number of cases of paralysis have followed tonsil and adenoid operations, and this bears out the idea that injury to mucous membranes may let the virus through to the nervous system.

Moreover, there is an impression that infantile paralysis occurs oftener than would be expected on the laws of chance in persons at certain times, when there are known

\*A "Green Lights to Health" broadcast given through Station WAAB by Dr. W. Lloyd Aycock on Wednesday, April 30, and sponsored by the Public Education Committee of the Massachusetts Medical Society and the Massachusetts Department of Public Health.

changes in the mucous membranes due to alterations in hormone secretion. These naturally occurring changes have been reproduced experimentally in monkeys. When these animals are given instillations of the virus in their nostrils, their resistance is seen to be different from that of normal animals. In addition to these experiments it has been found that children who have had infantile paralysis have different glandular secretions as compared with those who have not had the disease.

Thus, from all these studies, we may say that the exceptional occurrence of paralytic infantile paralysis among the many who are exposed to the virus is determined by individual susceptibility which is physiologic in nature and bound up with differences in certain of the endocrine glands. Infantile paralysis therefore, does not present the simple problem of a disease to which we can apply universal preventive measures such as smallpox in which we can vaccinate everybody, or rabies in which we can readily select the few who need vaccination—those bitten by a rabid animal. From the point of view of paralysis infantile paralysis is a disease of limited occurrence, and close attention must be paid to its behavior when the practicability of preventive measures is considered.

These talks are called Green Lights to Health. The green lights in infantile paralysis now seems to be in the direction of studying the question of susceptibility. If we are to be able to pick out the few who are susceptible, to try to understand what makes them susceptible and to learn how to correct their susceptibility in the hope of turning what is for them a distressing disease into what is for most people a harmless immunizing infection. For it may not be feasible to adopt too sweeping or drastic measures for the benefit of a few of the many who are exposed to the virus.

Now that knowledge has extended to the milder infections with this virus we can take some comfort, if an epidemic appears when we remember that over half the cases diagnosed do not develop paralysis, that probably half the patients who do develop paralysis recover entirely and that many of these are so slightly affected that they are not at all handicapped in following any of the ordinary pursuits of life.

## DEATHS

**CHRYSTAL**—MICHAEL H. CHRYSTAL, M.D., of Leominster died July 13. He was in his seventy-fourth year.

Born in North Adams, Dr. Chrystal received his degree from Baltimore Medical College in 1901. He was a member of the surgical staff of the Leominster Hospital and was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow and two sisters survive him.

**SMITH**—ALFRED C. SMITH, M.D. of Brockton died July 15. He was in his seventy-third year.

Born in Capetown, South Africa, Dr. Smith received his degree from Tufts College Medical School in 1898. He was a former president and treasurer of the Plymouth District Medical Society, and a member of the Massachusetts Medical Society, being a member of the Committee of Ethics and Discipline for many years, and of the American Medical Association.

His son survives him.

## NEW HAMPSHIRE MEDICAL SOCIETY

### DEATH

**CHEEVER**—NATHANIEL F. CHEEVER, M.D. of Greenfield died June 15.

He was born in Walden, Vermont, in 1856, graduated from the University of Vermont Medical College in 1883, and had practiced in Greenfield and the surrounding towns since 1884. He was a member of the American Medical Association and of the New Hampshire Medical Society, was prominent in fraternal organizations and held various town offices. He represented Greenfield in the Legislature in 1909-1911.

**KITTREDGE**—FRANK E. KITTREDGE, M.D., of Nashua, died July 8. He was in his eightieth year.

Born in Concord, Dr. Kittredge received his degree from the University of Pennsylvania School of Medicine in 1885. He had practiced in Nashua since 1889 and was one of the founders of the Nashua Memorial Hospital. He was a member of the New Hampshire Medical Society, the American Medical Association, the American College of Surgeons, the American Academy of Ophthalmology and Laryngology and the American Laryngological Rhinological and Otolaryngical Society.

## MISCELLANY

### RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR MAY, 1941

DISEASES	MAY 1941	MAY 1940	FIVE YEAR AVERAGE*
Anterior poliomyelitis	0	1	3
Chicken pox	12	1207	1107
Diphtheria	9	11	1
Dysentery	1284	1373	1211
Dysentery, bacillary	2	15	9
Cerebral measles	640	109	315
Conorrhoea	319	313	393
Lolal pneumonia	209	206	414
Measles	4117	4058	3846
Meningococcus meningitis	8	3	14
Scrub typhus	1479	943	1047
Paratyphoid B fever	12	22	25
Scarlet fever	827	670	905
Syphilis	437	518	473
Tuberculosis pulmonary	333	350	244
Tuberculosis, other forms	34	31	77
Typhoid fever	9	16	6
Undulant fever	158	8	4
Whooping cough	1158	757	684

\*Based on figures for preceding five years

### GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Diphtheria was reported from Acton, 1, Boston, 2, Brookline, 1, Cambridge, 1, Fall River, 2, Revere, 1, Watertown, 1, total, 9.

Dysentery, bacillary, was reported from Waltham, 1, Worcester, 1, total, 2.

Malaria was reported from Winthrop, 1, total, 1.

Meningococcus meningitis was reported from Brockton, 2, Chatham, 1, Fall River, 1, Hardwick, 1, New Bedford, 1, Quincy, 1, Taunton, 1, total, 8.

Paratyphoid A fever was reported from Chariton, 1, total, 1.

Paratyphoid B fever was reported from Cambridge, 1, Foxboro, 1, Lexington, 9, Malden, 8, Needham, 1, Waltham, 1, Worcester, 1, total, 22.

Pellagra was reported from Boston, 1, total, 1.

Septic sore throat was reported from Andover, 2, Beverly, 1, Boston, 8, Fall River, 1, Gill, 1, Merrimack, 2, Milton, 1, Oxford, 1, Scituate, 1, Williamstown, 1, total, 19.

Tetanus was reported from: Dudley, 1; Middleboro, 1; New Bedford, 1; total, 3.

Trachoma was reported from: Boston, 1; total, 1.

Typhoid fever was reported from: Arlington, 1; Boston, 4; Carver, 1; Leicester, 1; Medford, 1; Newton, 1; total, 9.

Undulant fever was reported from: Bridgewater, 1; Gloucester, 1; Leominster, 5; Milford, 1; Newton, 1; Pittsfield, 1; Shelburne, 1; Worcester, 1; total, 12.

German measles, measles, mumps, pulmonary tuberculosis, undulant fever and whooping cough show an increased prevalence, all being higher than the average for the five previous years.

Diphtheria, bacillary dysentery, lobar pneumonia and typhoid fever were reported less frequently than usual, all except the last being below the five-year average.

No cases of anterior poliomyelitis were reported during the month.

Meningococcus meningitis has been gradually increasing, but has not as yet reached the five-year average.

The incidences of chicken pox, dog bite, paratyphoid fever and scarlet fever were at about normal levels.

## NOTES

The following promotions on the faculty and teaching staff of the Harvard Medical School, effective next September, were recently announced: Donald L. Augustine, associate professor of comparative pathology and tropical medicine; William L. Aycock, associate professor of preventive medicine and hygiene; Harry C. Solomon, clinical professor of psychiatry; Charles G. Mixer, clinical professor of surgery; Robert S. Morison, assistant professor of anatomy; Thomas D. Jones, assistant professor of medicine; Aubrey O. Hampton, assistant professor of roentgenology; Arthur T. Hertig, assistant professor of pathology; Jacob Fine, assistant professor of surgery; Harold G. Tobey, lecturer on laryngology; Henry R. Vies, lecturer on neurology; Charles T. Porter, lecturer on otology; George G. Smith, lecturer on genitourinary surgery; Henry S. Bennett and Edward W. Dempsey, associates in anatomy; John L. Oncley, associate in physical chemistry; Mark D. Altschule, Howard F. Root and Eugene A. Stead, Jr., associates in medicine; Charles D. May, associate in pediatrics; Eric Lindemann, associate in psychiatry; John E. Dunphy, Franc D. Ingraham, Champ Lyons, Leland S. McKittrick and Augustus Thorndike, Jr., associates in surgery; and John H. Harrison and Fiorindo A. Simeone, associates in genitourinary surgery.

President Leonard Carmichael of Tufts College has recently announced that a fund, representing a fiftieth birthday present from over two hundred friends to Mr. Joseph F. Ford, a Boston manufacturer, has been turned over to Tufts College Medical School. It will be known as the Joseph F. Ford Student-Aid Fund, and the income will be used to help deserving students to defray the costs of medical education.

## CORRESPONDENCE

### "PRACTICAL ASPECTS OF SURGICAL SHOCK"

To the Editor: Dr. J. Englebert Dunphy's review of the shock problem in the May 22 issue of the *Journal* is neat and timely, but it would be unfortunate if his article were to spread an impression that observation of the pulse and of the arterial blood pressures fails to detect shock early.

Pulse rates were of no value, he and his collaborators have concluded in recently published experiments with barbiturized animals. Their published protocols show

fast control pulse rates, often 100 to 130. Many physiologists use only well-trained animals, to avoid the unnatural experimental conditions of narcosis, and they have shown the normal pulse rate of large dogs to be 60 to 80. Barbiturate narcosis has been shown to raise the pulse rate through sympathetic stimulation. But in any case, the protocols of Dr. Dunphy and his collaborators show rather immediate further elevation of pulse rates of burned or traumatized barbiturized dogs to maximums of 150 to 200 beats a minute. Even in barbiturized dogs, then, the pulse rate seems to react definitively in the early stage of shock. Their conclusion has no basis in fact; let them first show dogs approaching shock with pulse rates below 80.

More unfortunate is their error of calling the pressure recorded by an intra-arterial Ludwig mercury manometer "the blood pressure" in their text and "systolic pressure" in their tables. It is only the integrated mean arterial pressure, that is to say, the mathematical average of the changing pressures in a given artery during the whole heart cycle. Of course they, like everyone else, find that this mean pressure is well maintained throughout early shock, in the compensated stage of "diminished effective blood volume." The same sort of maintenance of mean pressure takes place in us every day when we rise from the lying to the standing position: at the same time the venous return and therefore the cardiac output diminish, the pulse rate rises very slightly, and the pulse pressure (systolic arterial minus diastolic arterial pressure) narrows definitely. Every physician who understands what he is studying when taking a Schneider index knows that he must observe the diastolic arterial pressure and that he should consider the systolic only in relation to it: he speaks of the blood pressures, not of the blood pressure.

Experimentally, investigators of the shock problem must discard the hoary Ludwig mercury column and must learn from physiology texts the meaning of diastolic arterial pressure. The use and necessity of a Huerthle spring-type or better a Hamilton membrane-type manometer deserve stress. It is easy to demonstrate with one of these that as soon as a small fraction—5 to 10 per cent—of the blood volume has been withdrawn, the pulse pressure narrows, usually with a distinct rise in diastolic and maintenance of mean arterial pressure. When small fractions are repeatedly withdrawn, the pulse pressure becomes progressively narrower and finally the mean pressure fails. This simple fact holds both in trained unanesthetized and anesthetized animals. It can be observed in any blood donor. I believe the experimental surgeons' persistent error in using Ludwig manometers should be called to account. Their continued inadequate concept and their thinking in terms of "the blood pressure" should no longer merit attention.

Experimental surgeons have slowly and laboriously gained a fruitful concept of "effective blood volume." This is qualitative at best. Now they urge universal adoption of hematocrit readings and red-cell counts and of falling-drop and plasma-protein determinations. These factors, in different stages and in different types of shock, change in varied directions. They, also, are qualitative when it comes to being interpreted. The surgeons still have to emphasize, perfectly correctly, that "correct appraisal of the condition [of the patient in shock] and the institution of proper replacement therapy are dependent on a careful study of the patient as a whole." Since the laboratory determinations which they recommend are not always reliably done even under the hothouse conditions of the experimental laboratory, and since they must be evaluated in a qualitative manner even by the expert, I urge a wider appreciation of the simple, mean-

ingful and quantitative determinations of the pulse rate and of the pulse pressure and the diastolic arterial pressure—the systolic pressure and the mean pressure are best forgotten. These measurements objectively check the all important clinical observation of the patient, especially his tongue, and the warmth and moistness and color and pulse quality of his extremities. Unlike hematocrit readings and plasma protein determinations, they are available to every practitioner and in every circumstance civil and military.

Physiologists have striven to avoid the qualitative and shifting sands of effective blood volume, albeit they neglect hematogenic, vasogenic and neurogenic types of shock. They do not speak of effective blood volume, but they quantitatively measure cardiac output. They show that during compensated shock the mean arterial pressure is well maintained, but the venous pressure and venous return (or cardiac output) are diminished. They teach that this measurable diminution, not the late drop in mean pressure of uncompensated shock, is the essential pathologic change. Pulse rate times pulse pressure gives an index which is a good serviceable first approximation of the cardiac output. No method of measuring cardiac output is ideal, not even the gas absorption methods or Hamilton's dye method. This last is to be recommended, nevertheless, in all investigations that include blood volume studies, for it can be combined with them easily without loss of accuracy to either measure. For clinical use, a diminishing series of products obtained by multiplying pulse rates by pulse pressures is an early, accurate measure of diminishing effective blood volume and impending shock. It can be interpreted in only one way unlike hematocrit readings and plasma protein determinations, it applies to shock of every stage and of every type and it requires only an attending physician with a watch and a sphygmomanometer.

Future study of shock ought to elucidate in what parts and to what degree the circulation is inadequate. The body extremities can be studied simply with oncometers, but conditions are easily vitiated by changes of body temperature. Visceral circulation studies are very painstaking and require trained unanesthetized animals and Rein's *Thermotromuhr*. These methods will teach us just how much various parts of the body are made to sacrifice their needed circulation to the end that the delicate brain cells and their jealous guardian the carotid sinus, receive a proper supply of oxygen and glucose, perhaps the kidney will be found to assert itself through its chemoregulators. As yet, we are ignorant of how much and for how long the various parenchymatous and vascular tissues can undergo oxygen deprivation and other metabolite insults. Real understanding of shock cannot come in advance of such studies.

Meanwhile the understanding observation of pulse rates and of blood pressures, both pulse and diastolic, deserves not less but rather more stress. If these objective measures have not been helping all of us, the fault is not in them but in ourselves.

ROBERT J. KINNEY, MD

512 East State Street  
Ithaca, New York

The above letter was submitted to Dr Dunphy, and the following reply was received:

To the Editor: Theoretically it is true, as Dr Kinney points out, that a diminishing series of products ob-

tained by multiplying pulse rate by pulse pressure is a measure of diminishing effective blood volume and impending shock. Perhaps it deserves more rather than less attention.

However, the tide of my review was Practical Aspects of Surgical Shock, and in actual practice, determinations of the pulse rate and pulse pressure are quite unreliable as a guide to fluid requirements in individual patients. To take a practical example during the course of some recent studies, 1220 cc of blood was removed in thirteen minutes from a volunteer subject. This constituted an actual reduction of the blood volume of over a quarter of the estimated total. Before removal of the blood, the pulse rate was 60, and the blood pressure 114 systolic, 75 diastolic. Four minutes after removal of the blood the readings were pulse 84 and blood pressure 110 systolic 80 diastolic. By no stretch of the imagination could these figures or even the difference between these figures be construed as evidence of a serious reduction of the blood volume. To a surgeon however, the loss of over a liter of blood may be of considerable importance and he must attempt to anticipate and correct such losses before significant alterations of the pulse and blood pressure occur.

This experiment is not a theoretical or hypothetical problem. The same thing occurs daily in surgical practice. To cite another example a patient recently entered this hospital seventeen hours after a free perforation of a duodenal ulcer. At the time of admission he was in evident peripheral vascular collapse. The pulse rate was 140 and the blood pressure could not be obtained. Following the administration of morphine and 1000 cc physiologic saline solution in the Emergency Ward the pulse rate was 110 and the blood pressure 105 systolic, 70 diastolic. Now a pulse rate of 110 and a blood pressure of 105 systolic 70 diastolic are not in themselves indicative of shock. Such levels are commonly observed under Avertin or spinal anesthesia without having any grave prognostic significance. Therefore, it is important that the hematocrit reading in this particular patient was 75 per cent and the serum protein 4.5 gm per 100 cc indicating an enormous reduction of the blood volume. Nearly 2000 cc of blood and plasma were required to restore this patient's hematocrit reading and serum protein level to normal, at the end of which time he had improved to such a degree that he withstood operation without difficulty. Over 2000 cc of fluid with a high protein content (3.8 gm per 100 cc) was found in the peritoneal cavity. Is a pulse rate of 110 and a blood pressure of 105 systolic, 70 diastolic, indicative of such an enormous loss of fluid?

In closing it is important to emphasize that determinations of the hematocrit and the plasma protein are quite simple procedures, readily done by any physician or technician capable of doing a red-cell count. The only expensive equipment needed is a good centrifuge. Finally, it should be stressed, as I emphasized in my review, that no laboratory procedures can supplant an accurate and careful clinical appraisal of the patient in shock. Examination of the pulse and blood pressure are procedures that will never be discarded and that often provide information of great value, but it is no longer correct to consider them infallible guides to the state of the circulation.

J. F. DUNPHY, MD

Peter Bent Brigham Hospital  
Boston

## REPORT OF MEETING

## NEW ENGLAND PEDIATRIC SOCIETY

At a meeting of the New England Pediatric Society, held on April 30 at Longwood Towers, Brookline, Dr. Samuel Levine, professor of pediatrics at Cornell Medical College, spoke on "Some of the Physiologic Peculiarities of the Premature Infant."

Dr. Levine began his talk by stating that the transition from intrauterine to extrauterine existence demands adaptations, and that premature infants make these adaptations less successfully, owing to their inadequate physiologic development. Charts were then shown of the causes of infant deaths: prematurity led, with 47 per cent, and birth injury and congenital malformations followed, with 14 and 10 per cent, respectively. The great preponderance of prematurity over any other single cause of infant death left little more to be said about the importance of the topic of discussion. It was further pointed out that even more significance should be attached to infant deaths as a whole, because of the present decline in birth rate.

The first physiologic system discussed by Dr. Levine was the respiratory apparatus. In this respect, it was shown that the premature infant was heavily handicapped, since five other systems may contribute to respiratory distress: the nervous system, by having a poorly developed gag and cough reflex; the vascular system, by decreased development of capillary circulation and thus more danger of atelectasis; the skeletal system, by weakness of the thoracic cage; the blood, because lowered fetal hemoglobin gives poor oxygen intake; and finally, the connective tissues, owing to lack of development of elastic tissues in the pulmonary vessels. The chemical stimulation of respiration in the premature infant is less sensitive than in the fully developed infant, the speaker reported; he showed a series of charts of his experiments in varied oxygen and carbon dioxide mixtures, which supported his statement.

Another very serious handicap to the premature infant, as compared with the full-term infant and the infant a few days after birth, was shown to be the delayed development of the capillaries of the medulla and lungs. Many slides were shown in which the capillaries, clearly demonstrated by the injection of dyes, were markedly inadequate in the medullae and lungs of premature infants. A well-graded series of these slides illustrated the speaker's next contention—that the capillary development of the lungs and medulla is proportional to the birth weight of the baby. The elastic tissue in the blood vessels was also found to be proportional to the birth weight of the infant.

The subject of bodily temperature was then taken up, and here again the premature infant was said to be badly handicapped because of a combination of several factors. Owing to incomplete muscular and systemic development, there is, first of all, low total-heat production. This is enhanced by the slow metabolism and consequent general inactivity of the infant. Inadequate use of calorogenic hormones (thyroxin and adrenalin) was also reported in premature infants, as well as poor sweating mechanisms on exposure to heat. One of the chief difficulties in heat regulation met by the underdeveloped infant was said to be due to the lack of proportion of surface area to body weight, the surface area being in considerable excess, and thus increasing loss of body heat. This, coupled with the insufficient amount of subcutaneous fat of the premature infant, dangerously impedes the retention of body heat. Dr. Levine showed results of his tests of heat conduction

in tissues of infants. These revealed that in spite of inadequate elastic tissues in the capillary walls, the premature infant had adequate heat conduction, better even than that of an adult, and hence that poor control of body heat was not due to a sluggish vasomotor system but to the large surface area and to the poor development of subcutaneous fat.

A study of water balance disclosed that the premature infant has an appreciable lowering in fluid output through the skin and lungs, as compared with the normal infant. A relatively greater burden is thrown on the kidneys. It was further found that the urea clearance is lower in premature infants, and increases with growth. The cause of the lowered urea clearance was found to be the decreased patency of the glomerular capillaries and the decreased development of epithelium of Volkmann's capsules. Impairment of kidney function was thus added to the list of handicaps to be met by the premature infant.

In the gastrointestinal tract, there are the problems of poor sucking, poor secretion of enzymes and, especially, poor absorption of fats. Premature infants were found to excrete more than the normal 5 to 10 calories per kilogram. However, carbohydrates and proteins were found to be metabolized satisfactorily, as evidenced by normal respiratory quotients and normal values for nitrogen absorption. This led to the practical suggestion that, to make premature infants increase weight most rapidly, fats should be replaced by carbohydrate and protein, instead of the usual custom of merely increasing the total number of calories in the diet.

There are several reasons for anemic tendencies in premature infants, such as deficient antenatal iron and copper storage, increased rate of neonatal blood destruction, incomplete development of respiratory enzymes and high incidence of digestive upsets. Hemorrhagic tendencies are present, owing to low prothrombin content of the blood and to weak capillaries, which are weakened further by poor elastic tissue.

There are several rachitic tendencies: reduced calcium and phosphorus storage, which is increased still more by the necessity of keeping premature infants indoors, rapid rate of growth, with a resultant drain on bone and other tissues, and decreased absorption of fats and fat-soluble vitamins.

Finally, Dr. Levine reported that vitamin C had been shown to have a specific effect in protein metabolism. As evidence of incomplete protein metabolism, he was able to demonstrate phenylalanine and tyrosine in the urines of premature infants; these substances were found in larger amounts when cow's milk was being used, because of the relatively high protein content of cow's milk. The oral administration of vitamin C, in the form of 100 to 500 mg. of levoascorbic acid, caused the disappearance of phenylalanine and tyrosine from the urine; hence, he concluded that it is advisable to administer vitamin C to premature infants soon after birth, especially if cow's milk is being used.

## BOOK REVIEWS

*Strange Malady: The story of allergy.* By Warren T. Vaughan, M.D. 8°, cloth, 268 pp., with 23 illustrations. New York: Doubleday, Doran and Company, Incorporated, 1941. \$3.00.

Any book that sets out to interpret science for the layman is as difficult to write as it is to review. How much knowledge should the writer expect his public to possess? How is he to present his subject so that it gives

balanced understanding? The reviewer, if he is a specialist in the same field, may quite justifiably think that some things are oversimplified and others not sufficiently explained.

Patients with allergy will get some understanding of their malady from Dr Vaughan's book. They will not, however, get a balanced point of view. Little space is given to the straightforward routine methods of study and to the simple, easily discovered environmental allergens that are the cause of the majority of symptoms. Perhaps to make the book more interesting, much emphasis is given to the dramatic, the rare and the complex.

There can be few patients so sensitive to nickel that symptoms of contact dermatitis occur from the amount of nickel that might be left in the skin from a needle used to give an injection hypodermically. Nor are there many patients who, having indigestion following the eating of chicken, can be relieved of their discomfort by enemas of chicken broth. Dr Vaughan describes the case of a patient allergic to grapes who had a rise in blood pressure of thirty to forty points if he drank a Martini cocktail, but a fall in blood pressure when he drank a Scotch highball. Another patient had sick head aches when he ate veal less than six weeks old. And still another was said to be so sensitive to sage pollen that he had hay fever if he ate mutton taken from an animal that had eaten sage.

The most fantastic note of all concerns a sailor who had an eagle tattooed on his chest. Cinnabar, which contains mercury, had been used for the eyes. When the sailor used mercury antiseptics, the eyes of the tattooed eagle were supposed to have become sore and eczematous. Why they were not continuously eczematous if the patient was really sensitive to mercury is not mentioned. And what the mercury antiseptic did to the lesion on which it was used is also not explained. Stories of this type will raise the readers' eyebrows oftener than they will carry conviction.

These examples are not culled from the book to discredit Dr Vaughan, whose reputation stands on a firm basis, but merely to show how dangerous it is to write a popular work unless one exercises great restraint. The lay reader would get some idea of the allergic processes but his picture of what an allergist does would not in any sense be a true one. It is a pity that the author's sense of the dramatic so overshadowed his scientific caution. Many of the examples given would be caviar not only to the general public but also to most practicing allergists.

*Studies on the Human Thyroid in Iceland* By Julius Sigríðsson 8°, paper, 130 pp., with 21 tables and 10 figures. Reykjavík: Premsmiðjan Edda H. F. 1940 6s

This book will be of interest to those who are concerned with problems of the thyroid gland. The size of the normal thyroid gland forms the subject of one chapter. Figures are given for the length, breadth, thickness and weight of the thyroid gland with comparative values for Germany and Iceland. The author concludes that the weight of the gland is a most significant feature. It is noted that the average weight of thyroid glands from Iceland and Japan is low.

The chapter concerning the history of iodine and the early use of iodine in the treatment of goiter is excellent. A discussion of methods for iodine analysis in this rod tissue is included, together with the method that the

author employed in his studies. The proportional and total iodine content of thyroid glands from Iceland is compared with that of glands from other districts. The values for Iceland are generally lower and compare with those found in Japan.

According to the author's results, the size of the thyroid gland increased when acute infectious processes had preceded death, in other diseased conditions, there did not appear to be any significant change.

The chapter on hyperplasia of the thyroid gland and its relation to iodine content is the best section of the book. This includes an excellent analysis of present theories, based on available experimental data, and emphasizes the viewpoint that hyperplasia of the thyroid gland indicates a relative iodine insufficiency. Whereas Marine has stated that the iodine content of the thyroid gland per gram weight is the important factor in the presence of colloid or hyperplastic thyroid tissue, the author believes from his studies that the total iodine content of the thyroid gland is a more significant figure. Since, in Iceland, the thyroid glands are smaller, the iodine content is less, and colloid goiter is rare, this difference in viewpoint is obvious.

*Surgical Anatomy of the Head and Neck* By John Finch Barnhill, MD, LL.D., and William J. Mellinger, MD. Introduction by Paul S. McKibben. Second edition, rearranged and revised. 4°, cloth, 773 pp., with 431 illustrations. Baltimore: Williams and Wilkins Company, 1940 \$15.00

The important change in the second edition of this work consists in the removal of the illustrations from a previous separate section, and their placement throughout the text where they can be consulted with ease.

The book furnishes a good comprehensive survey of the surgical anatomy of the head and neck, particularly from the viewpoint of the otolaryngologist. The material is covered in much greater detail than is usual in texts on general surgical or applied anatomy.

Although the conversational tone of the book, its arrangement about regional dissections and its rough but original drawings prevent the work from being concise, they do make it stimulating and rather charming.

*Diagnosis and Treatment of Menstrual Disorders and Sterility* By Charles Mazer, MD, and S. Leon Israel, MD. 8°, cloth, 485 pp., with 108 illustrations. New York: Paul B. Hoeber, Incorporated, 1940 \$6.50

It would be difficult to find a more comprehensive book than this on the subject of sterility and endocrine disorders peculiar to women. Not only are the abnormal manifestations of endocrine function as they apply to menstruation fully described and treatment suggested, but at the beginning of the book there are four chapters on the normal endocrine relations. The section on sterility is very complete, and when necessary, the description of the endocrine factors is repeated. In the sterility section, also, there is an interesting chapter that deals with habitual abortion. The diagnosis and treatment of male sterility and the technique of semen examination are included. Other tests, such as the tube test, endometrial biopsy and so forth, that are useful in the diagnosis of sterility are also described in detail.

There are many excellent illustrations and a well arranged index, a large bibliography is appended to each chapter.

Two criticisms should be made, although neither is particularly serious. The first is that, although a great deal of the material dealt with by the book is highly controversial, the authors tend to be somewhat dogmatic, and anybody using it must realize that the last word has not been said on many of these subjects. The other criticism is that the chapters on male sterility are written by Dr. Charles W. Charny, which seems to indicate that Drs. Mazer and Israel do not themselves check the husbands of their patients. The reviewer is convinced that an adequate picture of sterility in a couple can be obtained only when one man does the work-up on both partners.

In general, however, this book can be recommended highly, although its price will probably keep it off the shelves of anybody but the specialist in this field.

*Methods of Treatment.* By Logan Clendening, M.D., and Edward H. Hashinger, M.D. Seventh edition. 8°, cloth, 997 pp., with 138 illustrations. St. Louis: The C. V. Mosby Company, 1941. \$10.00.

This is the seventh edition of a text on treatment in internal medicine, first published in 1924. It is a summary of therapeutic procedure in one compact volume presented in the concise, lucid style characteristic of its senior author, Logan Clendening. Based both on material gathered discriminately from the ever-changing medical literature and on the wide clinical experience of the collaborating authors, all specialists in their respective fields, this work should be valuable to the general practitioner. The first part is devoted to methods of treatment in all its aspects, the second to their application to particular diseases. The work is well illustrated.

*Man's Greatest Victory over Tuberculosis.* By J. Arthur Myers, Ph.D., M.D. 4°, cloth, 419 pp., with 31 illustrations. Springfield, Illinois: Charles C Thomas, 1940. \$5.00.

This book deals chiefly with the remarkable accomplishments and progress made by veterinarians in the prevention of tuberculosis in cattle. Dr. Myers's main thesis is that a positive reaction to the tuberculin test signifies the presence of tuberculous lesions. Thus he extols the veterinarians for their steady insistence on the tuberculin testing of all herds and the elimination of the positive reactors. That the veterinarians have been successful in their task is attested by the fact that the entire nation is now an accredited area, which means that the number of cattle reacting to tuberculin is less than 0.4 per cent. Whereas in 1917 only 20,000 cattle were tested, 25,000,000 tuberculin tests were carried out in 1935.

This book consists of twenty-six chapters, very well written in a remarkably easy and fluent style. Each chapter has a good summary. The last chapter, entitled "Lessons for Physicians in Human Medicine," is apparently the real reason for the writing of the book.

The author, who has always been in the forefront of the fight against tuberculosis, has been the advocate of segregation and the more aggressive treatment of "open" cases of pulmonary tuberculosis. He has always been the opponent of those recommending immunization against tuberculosis with attenuated organisms (BCG). He stresses the fact that immunization has accomplished nothing so far as the prevention of tuberculosis in cattle is concerned, and that good results have been obtained only after all the positive reactors have been eliminated from the herd. Thus he deplores strongly the facts that physicians have done almost nothing to provide quarantine for

tuberculous persons, that they have allowed such persons to enter this country without adequate examination, and also that there is no ban on intercounty or interstate travel.

The author points out that a person reacting to tuberculin has definite tuberculous lesions, and hence has tuberculosis. Just what steps we should take in the prevention or treatment of such cases he omits to state. He apparently considers the preventorium to be of little or no value. He wishes only to direct attention to these matters, leaving their correction to the proper health authorities.

Veterinarians, particularly, should find this book interesting and instructive. In addition, it contains much material that should aid physicians in dealing with the many problems of human tuberculosis.

*A Handbook of Elementary Psychobiology and Psychiatry.* By Edward G. Billings, M.D. 16°, cloth, 271 pp. New York: The MacMillan Company, 1939. \$2.00.

This little book represents an attempt to summarize psychiatry from the psychobiologic point of view. The author has spent some time at the clinic of Dr. Adolf Meyer at Johns Hopkins, has acquired an understanding of his point of view and terminology, and has added to this the experience of working at the Psychiatric Department at the University of Colorado.

The chapters dealing with psychiatric examination procedures and with the descriptive material of the psychotic syndromes are by far the best. Brief and succinct methods are presented for obtaining the complete psychiatric history and mental status. The types of disturbed behavior encountered in psychiatric work are well described. It is in these that the reviewer believes that the major contributions of the psychobiologic school have been made. The emphasis on a good clinical study of the patient and on a careful and helpful observation of the patient is most creditable.

The chapter on psychobiology is an understandable presentation of an important point of view in psychiatry. It is well done, and its limitations are the inherent limitations of that approach and its terminology. The chapter on psychotherapy is clear, but little reference is made to data indicating the therapeutic value of the approaches suggested. Any therapeutic procedure, logical as it may seem, is only of interest and theoretical value unless it is supported by a series of cases proving its validity. The selected readings in Part V represent the basic writings in the field of psychiatry.

This book has value for the student, the internist, the surgeon and the psychiatrist. It fulfills the purpose of the author.

*Diseases Transmitted from Animals to Man.* By Thomas G. Hull, Ph.D. Second edition. 8°, cloth, 403 pp., with 45 illustrations. Springfield, Illinois: Charles C Thomas, 1941. \$5.50.

The nexus of bacteriology and clinical medicine is very adequately represented in the study of diseases common to animals and man. Their manifestations as disease forms, the distinctive immunologic variations and the manner of spread are all important to those seeking knowledge in this field. This volume in a compact form offers a wealth of information of this nature. The list of diseases is too long to enumerate, and each is prefaced by brief historical data of great interest.

The type and format are so outstanding as to merit distinct praise.



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## A FRACTIONAL BROMSULFALEIN TEST TO DETERMINE LIVER DAMAGE IN THE NONJAUNDICED PATIENT\*

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**D**ESPITE the large amount of work that has been done on the functions of the liver during attacks of jaundice, very little attention has been paid to the problem of residual liver damage after the patient has recovered. This is probably because the available methods have failed to show variations from normal in the majority of cases. During the last three years, 50 patients with disease of the liver have been studied in an effort to appraise the amount of residual liver damage, during and after convalescence, by frequent hippuric acid excretion, urinary urobilinogen, icteric index, total, free and ester cholesterol and lipid phosphorus determinations<sup>1</sup> and modifications of the bromsulfalein-excretion test.

Bromsulfalein has been in use for the last fifteen years and is generally considered the most satisfactory dye for determining liver function. Mills and Dragstedt<sup>2</sup> found that the mode of excretion of intravenously injected bromsulfalein is through the reticuloendothelial system, since blocking of these cells with India ink results in marked retention of the dye in the blood stream. Obstruction of the bile ducts does not impair the removal of bromsulfalein to the extent that it impairs bilirubin excretion.<sup>2</sup>

These authors have observed that removal of the dye in dogs appears to occur in two phases.<sup>2</sup> In the first five minutes after injection, 85 to 95 per cent of the dye is removed from the blood stream. A secondary or subsequent phase of varying length occurs after this five-minute interval, during which the remainder of the dye is excreted.

### METHODS AND MATERIAL

The hippuric acid excretion was determined by the method of Quick.<sup>3</sup> Normal human beings ex-

crete 2.5 to 3.0 gm. within four hours of the administration of 6.0 gm. of sodium benzoate. Urobilinogen in the urine was determined by the procedures of Watson<sup>4</sup> and Wallace and Diamond.<sup>5</sup> Normal persons excrete up to 4 mg. in twenty-four hours by the Watson method and show urobilinogen present in a 1:16 dilution by that of Wallace and Diamond.

Using the Rosenthal<sup>6</sup> technic, 2 mg. of bromsulfalein per kilogram of body weight was injected intravenously. A control blood specimen was taken just before the injection. One-half hour later, a specimen was obtained, rendered alkaline and compared with color standards.<sup>7</sup> Since it soon became apparent that patients only recently recovered from severe attacks of jaundice showed no retention of the dye after thirty minutes, a modification of technic was tried. Bromsulfalein levels in the plasma were observed at intervals of two, five and fifteen minutes. The two-minute sample showed such high levels in normal subjects that it was discontinued. In 10 normal patients at the end of five minutes, bromsulfalein retention was never in excess of 60 per cent, and the fifteen-minute sample rarely showed more than 5 per cent retention of the dye.

Other investigators have demonstrated the value of the fractional bromsulfalein test, although it has never come into common use. Rosenthal and Bourne,<sup>7</sup> using a fractional bromsulfalein test and the Wallace and Diamond<sup>5</sup> method for urobilinogen in urine on patients following various types of anesthesia, showed that a disturbance in function could be demonstrated with the bromsulfalein test long after pigment metabolism had returned to normal.

MacDonald<sup>8</sup> described a fractional bromsulfalein test using 2 and 5 mg. of dye per kilogram of body weight and taking blood specimens every

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‡Prepared by Hlyson, Westcott and Dunning, Baltimore.



TABLE 1. *Summary of Data.*

CASE No	DATE	BROMSULFALEIN RETENTION			ICTERIC INDEX	HIPURIC ACID EXCRETION gm	UROBIL- INOGEN* EXCRETION mg /24 hr	ADDITIONAL DIAGNOSIS	RESULT
		2 MIN %	5 MIN %	15 MIN %					
Acute Infectious Hepatitis									
1		10	5	3	7	4.1			Recovery
2		15	5	2	5	2.8			Recovery
3		25	15	0	7	3 "			Recovery
4	1/31/40		95	5	7		Trace	Glomerulonephritis	
	1/11/40		70	2	6		Trace		Recovery
5	2/8/40		42	3	6	4.0		Pancreatic abscess	
	2/24/40		18	2	6	4.2			Recovery
6			100	20	8		Trace		Recovery
7	5/4/40		100	60	30	1.1	Trace		
	5/16/40		80	35	10	1.7		Healing, subacute yellow atrophy	
	5/29/40		80	50	7				Illness continues
	6/20/40		100	10	6	2.8			
	8/1/40		85	20	7	1.4			
	10/26/40		100	90	12	1.2			
8			80	30	5	1.0		Circulation time 16 sec	Death of acute yellow atrophy
9			50	2	20	2.8			Recovery
10	9/3/40		100	55	25	2.7		Spontaneous abortion during height of jaundice	Illness continues
	10/24/40		65	40	8	1.7			Re entry for pyelitis
Acute Toxic Hepatitis									
11	2/27/39	60	20	0	10	3.7		Arsphenamine poisoning	Recovery
	4/22/39	3	0	0	8				
12		8	5	2	7	2.7		Sulfanilamide poisoning	Recovery
13		30	10	2	7	3.7		Carbon tetrachloride poisoning	Recovery
14			10	0	6	3.3		Arsphenamine poisoning	Recovery
15		10	5	3	8	4.1		Arsphenamine poisoning	Recovery
16	8/22/40		100	60	25			Carbon tetrachloride poisoning	
	8/27/40		90	25	10	3.0			Recovery
Chronic Cirrhosis									
17		5	3	0	6	2.9		Portal cirrhosis	Recovery†
18		9	4	2	8	2.5		Portal cirrhosis	Recovery
19		60	3	0	5	2.8		Portal cirrhosis	Recovery
20		60	40	40	7	1.6		Hemochromatosis	Death
21		30	15	2	7	3.8		Portal cirrhosis	Recovery
22		40	30	15	8	1.0	5.7	Portal cirrhosis	Death
23			5	2	8	3.4	0.2	Portal cirrhosis	Recovery
24			45	2	8	2.8		Portal cirrhosis	Recovery
25	11/1/39	100	100	80	8	1.1	0.8	Banti's syndrome	Illness continues
	5/13/40		100	90	15	2.1			
	7/13/40		75	25	30	0.7			Splenectomy
	8/1/40		50	40	12	Vomited			Re entry
	9/6/40		100	100	15	1.2			
26	1/10/40		100	20	8			Portal cirrhosis, pancreatitis	
	1/18/40		12	2	7				Recovery
	1/31/40		35	2	5	3.9			
27			70	35	6		Trace	Portal cirrhosis pellagra	Recovery
28	3/25/40		100	20	7		45.9	Toxic cirrhosis	
	4/11/40		25	5	7		3.7		
	5/1/40		100	70	10		18.9		Death
29			60	50	8		60.9	Portal cirrhosis	Death
30			70	40	8	2.5		Essential lipemia	Recovery
31			55	2	8	2.7		Beriberi heart disease	Recovery
32	5/22/40		35	30	6	0.8	15.0	Primary hepatoma	
	7/25/40		45	20	6	2.1		Portal cirrhosis	Death
33			60	30	6	2.2		Portal cirrhosis	Recovery
34	6/24/40		100	45	6	0.8		Heart disease (circulation time, 40 sec)	
	8/7/40		70	12	8	1.2		Cardiac sclerosis	Illness continues
35			80	40	5	1.8		Portal cirrhosis	Illness continues
36	7/18/40			55	7	0.7		Portal cirrhosis	Illness continues
	8/2/40		80	65	7	0.4			
37			65	10	5	1.0		Portal cirrhosis	Illness continues
38	7/25/40		45	5	6	0.1		Portal cirrhosis, beriberi	
	8/2/40		30	5	7	1.0			Recovery
39			70	35	6	3.2		Portal cirrhosis	Recovery
Hemolytic Jaundice									
40		30	5	2	50	2.6		Arteriosclerosis	Death
41		3	2	0	7	3.8			Recovery
42			42	7	35		Trace		Recovery
Obstructive Jaundice									
43			100	80	40	3.4		Biliary cirrhosis	Recovery
44	2/27/39	100	80	40	7	2.9		Stricture of common duct	
	4/22/39	20	0	0	6	2.9			Recovery
45			85	30	8	1.5		Carcinomatous obstruction, postoperative biliary fistula	Illness continues
Biliary Fistula									
46		30	5	2	7		0.2		Recovery
Essential Lipemia									
47		20	5	0	5	2.6			Recovery
Gall Bladder Disease									
48		30	7	2	7	2.2		Acute hepatitis (recent)	Recovery
49		3	0	0	7	3.0		Giardiasis	Recovery
50			90	10	10	1.6		Biliary cirrhosis	Recovery

\*Watson method

†Recovery in the cases of chronic cirrhosis means recovery from the attack of acute necrosis

five minutes for thirty-five minutes. The resultant curves are similar to those given here, but such frequent tests seem hardly necessary.

During this study, no effort was made to perform bromsulfalein-excretion tests during jaundice, — with the exception of cases of hemolytic anemia exhibiting jaundice, — since it has previously been shown<sup>9, 10</sup> that the retention of the dye closely parallels the retention of bile.

In the 60 patients included in this study, the diagnoses were as follows: acute infectious hepatitis, 10 cases; acute toxic hepatitis, 16 cases; chronic cirrhosis, 23 cases; hemolytic anemia, 3

Figure 1 represents the course of 12 cases of acute hepatitis of approximately two or three weeks' duration followed by recovery. It indicates the time relation between the various liver-function tests. Improvement occurred first in the ester fraction of the total blood cholesterol, then in the hippuric acid excretion and finally in the bromsulfalein retention. The initial rise in urobilinogen output early in the disease was followed by a drop associated with diminished bile in the bowel. After four to seven days of clay colored stools, a brown stool appeared at the time of clinical improvement. About two days later, there was a

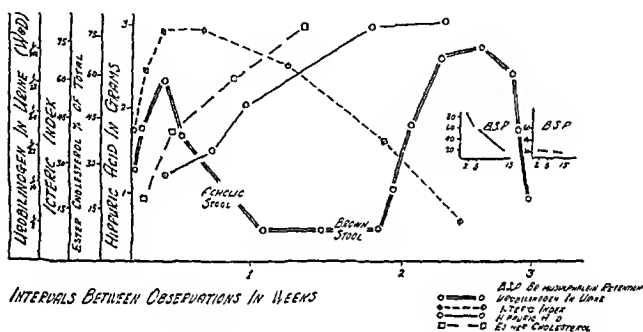


FIGURE 1 A Composite Chart of Serial Liver-Function Tests in 12 Cases of Acute Hepatitis with Recovery

cases; obstructive jaundice, 3 cases; biliary fistula, 1 case; essential lipemia, 1 case; gall-bladder disease, 3 cases

### RESULTS

In Table 1, the results are given for 73 tests in 50 patients with disease of the liver in whom more than one type of liver-function test was performed. Fractional bromsulfalein tests in 9 patients, or 18 per cent, showed abnormal retention when other tests were normal. Of these, 4 were acute cases (Cases 6, 7, 10 and 16); 3, cirrhoses (Cases 27, 30 and 39), and 2, obstructive jaundice (Cases 43 and 44). In Case 7, the bromsulfalein test still showed retention—90 per cent at fifteen minutes—five months after complete disappearance of the jaundice. In a case of beriberi heart disease (Case 38), the serial hippuric acid excretion was below normal, with a normal bromsulfalein excretion.

In 24 per cent of the patients, both the bromsulfalein retention and the hippuric acid or urobilinogen excretion were abnormal. In 58 per cent, both were normal.

secondary rise in the urinary urobilinogen that was usually higher than the first rise and sometimes persisted for two weeks. The interval between the first appearance of a brown stool and the abnormally increased urobilinogen excretion was quite variable, depending on the degree of liver damage. In a case of acute hepatitis lasting six to eight weeks, this interval may be ten days or more. This phenomenon might be due to a deficit in urobilinogen absorption by the liver.

A study of bromsulfalein excretion in 10 normal persons showed, in contrast to previous results in dogs,<sup>2</sup> that the dye retention at five minutes amounted to only 50 per cent on the average and never exceeded 60 per cent. The normal human being usually shows no more than 5 per cent retention at fifteen minutes.

Most patients recovering from acute diffuse liver damage show abnormal retention of bromsulfalein in both the early and late phases, improvement occurring first in the late phase. In this same type of case, although the fifteen minute specimen may show dye retention within normal limits, the five minute sample may show an abnor-

mally high value, describing a convex curve, and so indicate residual liver damage (Fig. 2). Results of this sort occurred twice in Case 4 and once in Case 7.

In chronic liver disease (Cases 20, 22, 27, 29, 30, 32, 33, 36 and 39), the early removal of the dye followed the pattern of normal persons, whereas the late phase was markedly impaired.

In a small group of cases of residual liver damage receiving sulfonamide therapy, falsely positive Wallace and Diamond tests for urobilinogenuria were obtained in about half the cases, owing to

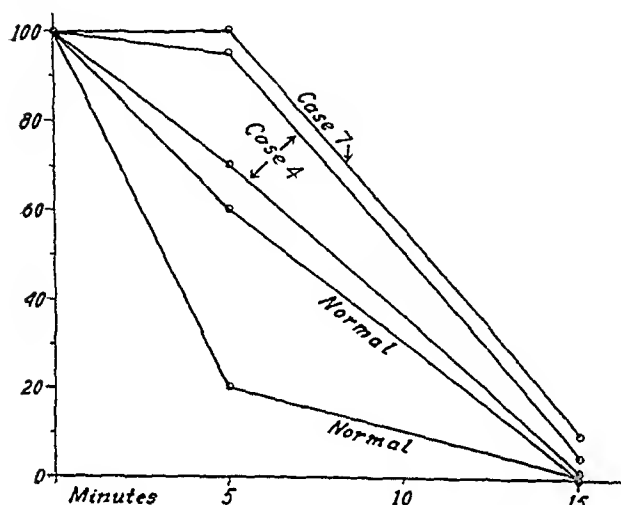


FIGURE 2. Normal and Abnormal Bromsulfalein-Retention Curves.

The percentage of retention is plotted against the time in minutes, following the intravenous injection of 2 mg. of bromsulfalein per kilogram of body weight. Note that the abnormal curves are convex.

chemical union of the sulfonamide and Ehrlich's aldehyde in the presence of an acid. In another small group of early to moderately advanced cirrhoses, normal levels of urobilinogenuria were noted in the presence of brown stools. In both types of cases, the fractional bromsulfalein test was of considerable help in distinguishing acute from chronic liver damage.

In Figure 3, the results are given for a fatal case of hemochromatosis (Case 20), which showed improvement in both the icteric index and ester cholesterol percentage during the course of the illness. During protamine insulin therapy, the hippuric acid excretion showed a slight improvement, but the patient shortly became incontinent, and it was therefore impossible to use this test. A fractional bromsulfalein test showed a curve characteristic of chronic liver damage. The patient became progressively worse and died five days later. Autopsy showed the typical findings of hemochromatosis.

In some patients, the hippuric acid excretion remains low at a time when the bromsulfalein

test is normal (Cases 22, 37, 38 and 48). A combination of these two tests is always better than either alone.

Two cases of congestive heart failure, pulmonary infarction and jaundice deserve discussion, although they are not included in this series. In spite of multiple tests, there seemed to be no way of determining the degree of liver damage because of the disturbance of circulation and its effect on function tests. At present, it is questionable whether there is any way of evaluating the state of the liver in the presence of circulatory failure associated with pulmonary infarction. One case showed disease of the coronary artery, with multiple pulmonary infarcts and with an icteric index of 80, and normal values for total and ester cholesterol and lipid phosphorus. Four hippuric acid excretion tests in the last three weeks of this patient's life were all below 1 gm. The second case of congestive failure was one of rheumatic heart disease and pulmonary infarction, with jaundice. Bile was absent in six urine specimens. The icteric index was 60, urobilinogen in the urine by the Wallace and Diamond method was repeatedly present in a dilution of 1:64, the hippuric acid excretion remained less than 1 gm., and the

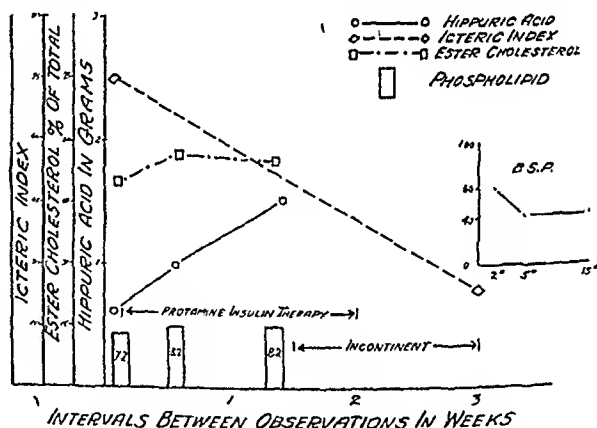


FIGURE 3. Liver-Function Tests in a Fatal Case of Hemochromatosis, with Acute Hepatitis.

fractional bromsulfalein showed 70 per cent retention at the end of five minutes, 40 per cent at fifteen minutes, 20 per cent at thirty minutes and 10 per cent at one hour.

In both cases, the elevated icterus is interpreted as being due to hemolysis associated with pulmonary infarction. From the delayed general circulation time associated with congestive heart failure, it may be assumed that there is some degree of impairment of the renal circulation—hence, the low hippuric acid excretion. With a slow circulation time, poor mixing of the intravenously injected dye may be present for fifteen minutes or more after injection.<sup>11, 12</sup> The fact that two

liver function tests and the icteric index may be disturbed by an extrahepatic process does not mean that these tests are worthless, but rather that they are only of value when used with good clinical judgment. It is fortunate that an estimate of hepatic function in the presence of congestive heart failure and pulmonary infarction with jaundice is not often necessary.

Another case, that of a failing nonjaundiced seventy-year-old patient (Case 8), was studied because of possible liver damage. Her downhill course could have been ascribed to generalized arteriosclerosis, hypertension and cardiovascular syphilis. With a normal circulation time, the bromsulfalein excretion showed 80 per cent retention after five minutes, and 30 per cent after fifteen minutes. Only 1 gm of hippuric acid was excreted. The two latter findings were the only laboratory evidence of hepatic insufficiency. The icteric index was 5, and the determination of the twenty-four hour urobilinogen excretion in the urine was within normal limits. At postmortem, the liver showed healing acute yellow atrophy.

#### COMMENT

From this study, it is evident that a certain small percentage of previously jaundiced patients show abnormal retention of bromsulfalein in the blood stream for periods varying from several weeks to several months following recovery. The abnormality is best revealed by a study of the serum at intervals of five and fifteen minutes rather than the customary thirty minute period, since the longer interval usually shows a normal result. A convex curve indicates residual damage even when the fifteen minute specimen shows no retention.

Soffer and Paulson<sup>12</sup> have shown that the bilirubin excretion test is a better test of residual liver damage than the half hourly bromsulfalein test. I have had no experience with the bilirubin test because of its expense, but it would be of interest to compare the bilirubin and fractional bromsulfalein tests in the same patients. Another advantage of the fractional bromsulfalein test is that its performance requires only fifteen minutes, compared with four hours for the bilirubin test.

A discussion of the hippuric acid excretion test on a similar series of cases has already been given in a previous report,<sup>1</sup> so that it requires no further comment.

#### CONCLUSIONS

A modification of the routine bromsulfalein test has been tried and includes the collection of

specimens at five and fifteen minutes. In a small group of patients, residual liver damage may be detected for periods varying from several weeks to months after jaundice has subsided. In 50 cases in which other liver function tests were used, the fractional bromsulfalein test showed abnormal function in 18 per cent when the other tests gave normal values.

A combination of the fractional bromsulfalein and the hippuric acid test is preferable to the use of either alone.

The test was not affected by variations in hydration or by kidney disease. In 3 cases of hemolytic anemia with jaundice, approximately normal results were obtained. The short time required for the fractional test is a distinct advantage.

Congestive heart failure, with its accompanying poor circulation time, makes the results of this fractional test unreliable, because of the prolonged mixing time of the dye in the general circulation, and also confuses the hippuric acid test, because of poor renal function.

Since this paper was submitted for publication, an article by Lucin and Aggeler (*Am J M Sc* 201:326-340, 1941) has appeared in which the rose bengal test has been modified in much the same manner as suggested here for the bromsulfalein test, and in which the new method is compared with the hippuric acid test.

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## THE MANAGEMENT OF A BLOOD BANK AT THE MASSACHUSETTS MEMORIAL HOSPITALS\*

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AT a recent clinical meeting of the Boston Surgical Society, considerable interest was shown in the technical management of the blood bank at the Massachusetts Memorial Hospitals. The questions and discussions arising in that demonstration prompted the writing of this paper. No attempt is made to review the history of this subject. A recent survey of the literature on blood banks, with an excellent bibliography, is presented by Douglass.<sup>1</sup>

There are very few active blood banks in New England. The reason for this may be the fallacy that the management of a bank requires the services of several full-time technicians, as well as the expenditure of large sums of money. I shall endeavor to prove that this idea is wrong.

A blood bank must have concrete reasons for its existence and demonstrable evidence of its value. The experience of the Massachusetts Memorial Hospitals is that a blood bank provides immediate availability of blood of various types, a safe blood from the standpoint of the transmission of syphilis, an economical blood (the cost of our transfusions has been materially reduced), a means for the collection of plasma (our outdated blood is converted into and stored as plasma), a lightening of the labors of the visiting staff and interns, and an increased efficiency in collecting blood. Furthermore, it places the responsibility of all transfusions on a director and his associates.

The blood bank at the Massachusetts Memorial Hospitals is made up of two component parts: placental blood bank and adult blood bank.

The placental blood bank was described in a previous article.<sup>2</sup> The bank was instituted in March, 1938. Since the development of the adult blood bank, the placental blood has been used for only two purposes: first, as a source of blood for newborn babies and pediatric cases and, secondly, as a source of blood for plasma.

The management of the adult blood bank is described in detail because of the many requests for this information from hospitals throughout New England.

### PERSONNEL OF THE BLOOD BANK

*Director.* A staff member interested in the subject of transfusion assumes the entire responsi-

bility. He selects and supervises the other members of the transfusion service and manages the blood bank. The director should also stimulate research and progress in regard to transfusions and blood banks.

*Operator.* The operator or his alternate physically examines all donors and personally performs all venepunctures for the collection of the blood. In this way, an efficient technic is developed.

*Technician.* A technician has been chosen to specialize in the work of the blood bank. She is a member of the routine laboratory force. The technician is a full-time laboratory worker, and although the duties of the blood bank are her primary interest, she is available for other work. Her duties consist in making hemoglobin determinations and complete blood counts on all donors and personally securing the samples of blood for serologic tests and typing; after collecting the samples, she personally completes their analysis and is responsible for recording all results on the various tags and cards. She also sees that all outdated blood is forwarded to the laboratory for siphonage, and that the plasma is returned to the refrigerator. At the most, this requires three hours a day.

*Running nurse.* The running nurse is a graduate nurse assigned to the two examining rooms where the clinics for the collection of blood are held. Her station at the clinic is permanent. She has, of course, many other hospital duties, but the blood bank is her chief responsibility. She is schooled in the technic, and it is her duty to see that all apparatus used in the collection of blood is in working order. She prepares the donor, and secures the history and permits before blood is taken.

*Supervising nurse.* The supervising nurse is a graduate and a member of the training-school office. She is responsible for all dispensing of blood: house officers are not permitted to remove blood from the bank without her permission during the day or without that of the supervisor of nurses on duty at night. It is her duty to see that the blood nearing the outdated period is dispensed first. Each day, the supervisor checks the refrigerator for temperature, and places on the upper shelves the bloods that have been liberated by completed serologic tests and typing. She tests all bloods for time limits, keeps the filing system in order, no

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tifies the cashier when a patient is to be discharged and has not met his obligation to the bank, and prompts the interns to secure donors for patients who have been given blood but have replaced none in the bank. Briefly, the supervisor keeps the bank solvent, and is responsible only to the director.

#### COLLECTION OF BLOOD

The two-unit system is used for the blood-collecting clinic: in one room the donor is questioned and examined, and in the other the blood is collected.

*Room No. 1.* In the history, special emphasis is placed on exanthemas, syphilis, malaria, allergy, tuberculosis, and the time of the last meal and the last transfusion. The donor is prepared on the operating table, with the arm extended on an arm board.

In addition to physical examination, which includes examination of the throat, skin and lymph nodes, the blood pressure, pulse and temperature are taken and a hemoglobin determination and complete blood count are performed. These data are filled in under the heading "Donor" on a special sheet prepared for the transfusion service. This sheet is yellow, as are all records pertaining to the transfusion department. The top of the sheet concerns the history of the recipient and is filled in at the time of transfusion. It consists in data that may be interesting from the standpoint of statistics: the indication for the transfusion, the method used, the amount of blood, the type of blood and the reactions, if any. The serial number is placed on each flask, and a corresponding number on a set of records pertaining to that flask, so that at any time during the year the exact number of transfusions given may be instantly determined. It is hardly necessary to state that if, for any cause, the physical examination or history brings to light some reason why the blood should not be used for transfusion, the donor is excused.

A written permit on a special blank is secured from the donor, giving permission to administer the blood to the patient mentioned in the permit. The permit also states that if, for any reason, the blood is not compatible or is not used for the patient for whom it was secured, the hospital may employ the blood for any other purpose it may see fit. This permit is witnessed.

*Room No. 2.* The closed system for collecting blood is used. The apparatus includes an aluminum pan (Wearever, No. 2434) wrapped in a sterile covering and containing a three-holed rubber stopper, through which there is a piece

of straight glass tubing 10 cm. in length. To this is attached a piece of stiff brown-rubber tubing with a 3-mm. lumen. In the other end of this tubing is inserted a Murphy drip bulb, without the air vent, and to the other end of the Murphy drip bulb, in turn, another piece of tubing is attached. Cotton is placed in the Murphy drip bulb. The operator applies suction by water pump or by mouth to the free end of the tubing. In the second hole of the rubber stopper is placed a right-angle glass tube, and to this is attached a piece of yellow, translucent, acid-cured rubber tubing 65 cm. (26 in.) in length with a 4-mm. lumen. This tubing is directly connected with a 13-gauge or 16-gauge needle, the taking needle. A glass adapter is purposely not used because it causes both constriction in the pipe line and frequent clotting. The translucent tubing serves the same purpose as an adapter, since blood may be

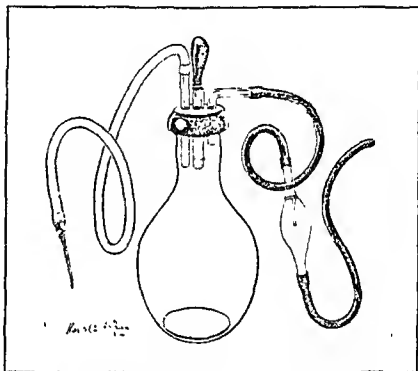


FIGURE 1. Apparatus Used for Securing the Blood.

visualized through the wall of the tubing. In the third hole of the stopper, there is a short section of glass tubing the free end of which is covered with a medicine-dropper bulb. This has been arranged so that if at any time it becomes necessary to add additional citrate to the blood it may be done by inserting a syringe needle through this bulb; by this method, it is unnecessary to detach the stopper. In the aluminum pan, there is also a Fenwal metal and rubber cap, which is inserted in the neck of the bottle at the completion of the collection of the blood, thereby keeping the contents of the bottle airtight. The 500-cc. Fenwal flask in which the blood is collected has a separate sterile wrapping.

After the collecting outfit has been assembled (Fig. 1), a 50-cc. ampule of 2.5 per cent sodium citrate solution is emptied into a sterile glass con-

tainer. By suction, this fluid is drawn into the collecting flask through the needle and the rubber tubing; the flask is then agitated so that its wall is wet by the solution. This amount of sodium citrate is usually sufficient to prevent the coagulation of 450 cc. of blood. If smaller or larger amounts are to be drawn, the volume of citrate solution is varied accordingly.

The Fenwal flask, with its attachments, is placed on a stand below the level of the donor and out of his line of vision—it is important, for psychic reasons, not to allow the donor to see the amount of blood removed. During the collection, the agitation of the flask is minimized. When the desired amount of blood (usually 500 cc.) has been collected, a hemostat is applied to the translucent tubing close to the flask. This tubing is then detached from the glass tubing in the rubber stopper. Samples of blood are collected in two test tubes for serologic tests and typing by simply releasing the hemostat for the tubing. The needle is then removed from the vein. The three-way rubber stopper is removed from the flask, a sterile pipette is inserted, and a sample of the blood and preservative is withdrawn and placed in the third test tube. This test tube is known as the pilot tube, and it is from this tube that all future typing will be performed, thereby eliminating the necessity of entering the flask until it is used for transfusion or its conversion into plasma.

After the completion of the collection of blood, 25 cc. of a 50 per cent solution of dextrose and 25 cc. of distilled water are gently added to the flask containing sodium citrate and blood. When dextrose is added in this amount, the supernatant fluid usually remains perfectly clear and shows no evidence of hemolysis for as long as forty-six days. However, when this preservative is used, the flasks are routinely forwarded at the end of twenty-one days for siphonage to convert blood into plasma. Blood preserved with sodium citrate alone is converted into plasma at the end of eight days.

The refrigerator in which the blood is stored is of special design (General Electric Company, Cabinet No. 2425). With thermostatic control, the temperature is maintained at 38°F. The revolving shelves are very practical, since one thus has access to any flask on the shelf without moving or agitating the containers. The flasks of one type are grouped together on a single shelf. Flasks most recently collected are placed on the lower shelf, to be distributed later when the laboratory work is completed. The refrigerator is located in the room in which the blood collections are made.

## PROCESSING OF PLASMA

From a blood collected to process into plasma, the latter is removed twenty-four hours later, and from blood that had been intended but had not been used for transfusion, on a definite date after collection. When the bank was instituted, a combined siphon and centrifuge method was used. The centrifuge process has been eliminated because the increased yield of plasma was not sufficient to compensate the risk of contamination by an added step in technic.

A very compact and economical cabinet has been constructed to be used while the plasma is being processed. The cabinet is a workbench with a hood attached. In front of the technician is a hinged glass window to prevent breath and dust contamination. Beneath the window is a 20-cm. opening to admit sterile gloved hands. A sterile gown is worn. The top of the hood is closed to eliminate active currents of air. Attached to the upper part of the hood is a Westinghouse Sterilamp.\* The cabinet is portable and should be placed in a clean room away from traffic.

The transfer of plasma from the blood flasks to the pooling flask is carried out in a closed system. The Fenwal stopper is removed from the flask of blood. A two-holed rubber stopper is substituted. A glass tube passing through one opening is adjusted to a level just above the line of demarcation between plasma and cells. The second glass tubing acts as an air vent. A 2-liter Fenwal flask is used for pooling the plasma. This large flask is connected to the flask of blood by rubber tubing. A two-holed rubber stopper is inserted in the pooling flask, and through the second opening is a glass tube with a rubber-tube attachment for suction. Suction is produced either by water pump or by mouth. Plasma is separated from bloods of various types and collected in the pooling flask. The flask is agitated, and the process is reversed to transfer the plasma from the pooling flask to the storage bottle.

Merthiolate (Lilly) is added to each batch of pooled plasma. A 1 per cent stock solution is prepared by adding 1 gm. of Merthiolate, together with 1.4 gm. of borax as a buffer, to 100 cc. of distilled water; 1 cc. of this solution is added to every 100 cc. of plasma. A sample of each batch of

\*The Westinghouse Sterilamps are essentially monochromatic generators of ultraviolet radiation, which is highly bactericidal. The tube is set for a radiation of 28.8 microwatts per minute as measured, by a Tantalum photoelectric cell. The tube is checked monthly, and if the intensity drops, the regulator may be adjusted to maintain a constant intensity. The tube is placed 75 cm. (30 in.) above the table. The ultraviolet ray will not penetrate glass, and therefore does not affect the blood, or the eyes of the technician. In preparation for processing the plasma, a sterile drape and then the flasks and apparatus to be used are placed on the bench. The Sterilamp is lighted, and after half an hour, the technician begins her operation, working under the lighted lamp.

plasma is obtained for culture, and the latter is incubated for at least two weeks.

The plasma is stored in the refrigerator in 500-cc. straight-walled flasks sealed with Fenwal rubber and metal caps.

The pooled plasma can be used without typing and will keep indefinitely if stored in an airtight container at 38°C. without exposure to light.

### BANKING

*Credit.* Seventy per cent of cases needing transfusion can be predicted days before the actual administration of the blood. These patients are requested to have one or more donors, according to the need, report to the blood clinic at a scheduled time. The blood is collected irrespective of type, and to this patient is credited the amount donated. If for any reason the full supply of blood collected is not used, it becomes the property of the bank.

*Debit.* If, because of an emergency, a patient is required to have a transfusion, the blood for which has been furnished by the bank, this patient is in debt to the bank for the amount given and must secure donors for the next banking day. The filing system compiled by the supervisor is responsible for keeping the bank solvent.

*Banking hours.* It is the policy of the blood bank to collect on certain afternoons and evenings. This variation in time allows for different working hours of the donors and has worked out very satisfactorily. No blood is secured from donors at any other time, except in emergency.

*Cost of transfusion.* A flat charge is made for each transfusion according to the means of the

patient. This charge is comparable to any operating-room fee. Many indigent patients who are unable to secure donors for one reason or another are now transfused without expense to the hospital. The availability, the safety and the decreased cost per patient have materially increased the number of transfusions. As plasma becomes available, there will probably be an increasing trend toward its use.

### SOCIAL ASPECTS

Approximately 5 per cent of unsuspected positive serologic reactions with bloods from donors have been encountered. Afflicted donors are requested, in a carefully worded letter from the social-service department, to return to the hospital. The reason for this conference is not divulged. The social-service worker verbally informs the donor of his misfortune and arranges for his treatment.

### SUMMARY

The management of the blood bank at the Massachusetts Memorial Hospitals is outlined. Emphasis is placed on specialization in the collecting and handling of the blood and the processing of the plasma. Experience with a blood bank has shown that the cost of the personnel and equipment is not prohibitive, that the ease and frequency of transfusion are increased, and that the safety factors of transfusion are greatly improved.

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## AN EVALUATION OF PERITONEOSCOPY\*

With Particular Reference to the Diagnosis of Abdominal Tumors

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**P**ERITONEOSCOPY, or visualization of the abdominal cavity, is far from new. However, following increased experience with an improved instrument, it is pertinent to inquire into the results that have recently been obtained. The physician wishes to know when peritoneoscopy is worth while and what information it provides that cannot be obtained in other ways. He wishes to know how much discomfort, expense and risk it involves for his patient. He wishes particularly to know how often the information obtained will materially alter the treatment.

It is not generally appreciated that this method of abdominal diagnosis is thirty-nine years old. The historical aspects have already been well reviewed by Ruddock.<sup>1</sup> In 1901, Kelling,<sup>2,3</sup> of Dresden, first demonstrated the observation of abdominal viscera on a dog, using pneumoperitoneum and a cystoscope. He later examined 2 patients by this method, one a case of ascites and the other a case of gastric carcinoma. Jacobaeus<sup>4</sup> developed an improved instrument and used the same technic. To illustrate the type of work done by these pioneers, Jacobaeus's report in 1913 of 138 such examinations included the diagnosis of 17 cases of liver cirrhosis, 31 cases of malignant abdominal tumor, 10 cases of tuberculous peritonitis, 3 cases of syphilitic liver and 9 cases of Pick's disease. Nordentöft<sup>5</sup> reported in 1912 the endoscopic examination of female pelvic organs with the patient in the Trendelenburg position. The instruments then used were too short to be certain of inspecting both the upper and the lower abdominal cavity through one insertion, had a narrow field of vision, and did not permit obtaining a biopsy.

These faults were overcome in the Ruddock<sup>1</sup> instrument, which has been in use for six years. Ruddock has reported 500 examinations with it, and is soon to report 1000 additional examinations. There is no other series nearly so large, but Benedict<sup>6,7</sup> has reported 50 and later 100 cases, and Thieme<sup>8</sup> last year published a critical survey of peritoneoscopy, based on 50 cases. The following data are based on 75 cases.

## METHOD

The detailed description of technic has been well covered by Ruddock<sup>1</sup> and is therefore only briefly outlined. A small block of the abdominal wall, preferably in the mid-line just below the umbilicus, is anesthetized by novocain infiltration. A 1.5-cm. skin incision is made. A pneumoperitoneum is induced with a small blunt trochar and cannula. A larger trochar with cannula, the latter constituting a sheath for the optical instruments, is then introduced through a nick in the anterior fascia. The instrument thus comes to lie in the space created by the insufflated air, between the abdominal wall and the abdominal viscera.

In the average case, inspection reveals the anterosuperior surface of the liver and variable amounts of the inferior liver surface near the edge. The dome of the gall-bladder fundus can almost always be viewed. The lower anterior gastric surface is seen. How much of the upper stomach is visualized depends on the degree of ptosis. The anterior surface of the great omentum and the surface of those coils of bowel not covered by it may be inspected. The pelvis can be well explored only with the patient in a very steep Trendelenburg position. In women, the uterine fundus, proximal tubes and anterior surface of the broad ligaments are readily seen. The fimbriated ends of the tubes and the ovaries may at times be prolapsed behind the broad ligaments; in these cases they are difficult to see.

The ambulatory patients in my series have averaged a thirty-six-hour stay in the hospital. In a few cases in which there was no biopsy, the patients have remained only ten hours. With increasing experience, I am convinced that there should be negligible discomfort, comparable to a well-executed abdominal paracentesis. To accomplish this, three things are necessary. First, the block of the abdominal wall, at least 5 cm. square, must be thoroughly infiltrated, with particular attention to using sufficient novocain beneath the fascia and below each rectus muscle to anesthetize the peritoneum. Secondly, the optical instrument must be gently moved, so that it does not jolt and, if possible, does not touch visceral surfaces. Thirdly, an effort must be made to press out most of the air at the end of the examination.

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For satisfactory results, the facilities of an operating room are needed. An operating table that will tip steeply either way, suction and electrocautery are recommended.

I have at various times inserted the instrument into each of the four quadrants of the abdomen and the epigastrium. The cardinal rule is to keep far away from old laparotomy scars to which the hollow viscera might be adherent. The literature records a few cases of penetration of bowel due to an adherent viscus; all were detected and none were fatal. It is imperative that the pneumoperitoneum needle move freely within the abdomen to ensure that no emphysema of omentum or of abdominal wall occurs.

#### CONTRAINDICATIONS

Peritoneoscopy should never be used in the possible presence of bacterial infection in the free peritoneal cavity. Except in the diagnosis of ectopic pregnancy (Hope<sup>8</sup>), it has no place in the diagnosis of acute abdominal conditions. It has been used to see if an abdominal wall stab wound penetrated through the parietal peritoneum (Hamilton<sup>10</sup>). This seems safe only in an early case, and then only with preparations to follow at once with a laparotomy if penetration through all the layers of the abdominal wall has occurred. The pneumoperitoneum may produce some reduction of vital capacity. If there is an appreciable amount of hydrothorax, the fluid should be removed before peritoneoscopy. Naturally, decompensated heart disease is a contraindication. Age and senility alone are no contraindication. 14 of the patients in this series were over the age of sixty, and 2 were over the age of eighty.

#### COMPLICATIONS

In the 75 cases, there has been no mortality attributable to peritoneoscopy. There has been no complication since the second case, in which sepsis occurred in the abdominal wall as the result of contamination from the wound of a previous piracentesis. Complications listed in the literature are emphysema of the abdominal wall,<sup>6</sup> hematoma in the wound of entrance<sup>8</sup> and bleeding from the site of biopsy.<sup>1</sup> Hematoma in the abdominal wound in cases with liver damage may be prevented in the future by use of vitamin K. Electrocoagulation of biopsy sites must be carefully performed if any appreciable bleeding occurs.

#### FIELD OF USEFULNESS

There are four broad groups of conditions in which peritoneoscopy may confirm a diagnosis, render an exploratory laparotomy unnecessary, and

aid materially in giving a prognosis, namely, to determine the presence, extent, nature and operability of cancer, to demonstrate the nature and extent of pelvic tumors and of lesions of the female pelvic organs, to make the differential diagnosis of ascites, and to make the differential diagnosis of liver disease. Naturally these groups overlap. In this series, the following diagnoses were correctly made:

DIAGNOSIS	NO OF CASES
<b>Malignancy</b>	
Metastatic carcinoma in the liver	11
Peritoneal carcinomatosis	6
Gastric carcinoma, without metastases	5
Metastatic fibrosarcoma of the peritoneum	1
Melanotic sarcoma in the liver	1
Primary hepatoma of the liver	1
<b>Tumors of the female pelvic organs</b>	
Ovarian carcinoma	7
Malignant ovarian cyst	1
Benign ovarian cyst, with twisted pedicle	1
Benign ovarian cyst	1
Fibroid uterus	1
<b>Differential diagnosis of ascites and liver disease</b>	
Cirrhosis of the liver	14
Syphilis of the liver	1
Splenomegaly, without cirrhosis	1
Fatty infiltration of the liver	1
Inflammatory mass below the liver	1
Carcinoma of head of the pancreas (presumptive)	1
Tuberculous peritonitis	1
Multiple adhesions	1

In the remaining 18 cases, peritoneoscopy showed the visualized portion of the abdominal cavity to be normal. These patients had hypernephroma, calcified mesenteric masses, retroperitoneal tumors, vaginal carcinoma, rectal carcinoma and so forth. Two obese patients, thought probably to have abdominal tumors, were shown to have none.

Early leaking of blood from an ectopic pregnancy is diagnosable with great accuracy.<sup>9</sup> The peritoneoscope has been used to sterilize the female by electrocoagulation of the isthmal portion of the Fallopian tubes under direct vision (Anderson<sup>11</sup>). This attempt at operative peritoneoscopy has even been carried farther in suturing the internal orifices of inguinal hernia under direct vision (Ruddock, quoted by Sawyer<sup>12</sup>). It seems that these operative procedures are more surely and safely performed by laparotomy. However, I have had no personal experience on which to base such a conclusion.

#### ACCURACY OF DIAGNOSIS

There is no case in which I am, as yet, aware of an erroneous diagnosis; biopsies were obtained

in 15 cases. In 2 cases, however, a conclusive diagnosis could not be made. One patient was a man with ascites who previously had had extensive gastric surgery for peptic ulcer. Because of numerous adhesions, only a small portion of the right upper peritoneal cavity and liver surface was available for inspection. In the second case, a carcinoma of the gall-bladder area was suspected, but the omentum had become densely adherent to both gall bladder and liver, and hence a satisfactory view could not be obtained. In the second case, exploratory laparotomy was advised and performed, and a carcinoma of the gall bladder, with metastasis, was found.

Thieme<sup>8</sup> has pointed out that the largest groups of cases for peritoneoscopy are those in which the diagnosis is already strongly suspected and only absolute confirmation is wanting. There is another small group of cases in which every diagnostic procedure short of exploratory laparotomy has failed to give the diagnosis. In these cases, the result of peritoneoscopy may be quite dramatic. Case 1 is illustrative.

CASE 1. Mrs. B. B. (J. H. P. D. H. 5350), a 46-year-old housewife, entered the hospital complaining of weakness and fullness in the pit of the stomach for over a year. One year previously, she had had frequent and profuse menstrual periods and had been examined at a clinic, where fibroids were found. Five months before entry, she became troubled by indigestion, and the vaginal bleeding ceased. Four weeks prior to entry, she had lancinating pain in the right upper quadrant lasting for several hours. There had been definitely increasing dyspnea on exertion. Physical examination showed a palpable liver, a fibroid uterus, a slight anemia and a slight and irregular fever. X-ray examination of the gall bladder, stomach and colon was negative. On entry, x-ray films of the chest were negative, but later showed fluid in the right chest.

Peritoneoscopy confirmed the diagnosis of a fibroid uterus. The stomach, omentum and peritoneal wall were normal, but on the superior surface of the liver two yellow nodules, several centimeters in diameter, were seen that had the appearance of metastatic carcinoma. A biopsy report indicated carcinomatous metastasis to the liver; the primary source was not known. This patient gradually failed and died.

In this patient, x-ray examination and all other diagnostic studies failed to give the diagnosis, yet metastatic carcinoma was present. Two other cases were identical.

In 2 cases, intra-abdominal cancer was strongly suspected, but peritoneoscopy fortunately proved the presence of benign lesions. One was a case of syphilitic liver, and the other an intraomental abscess of unknown etiology; an abstract of the latter follows.

CASE 2. J. G. (J. H. P. D. H. 327-395), a 40-year-old Lithuanian, entered the hospital complaining of steady pain in the right upper abdomen of 10 days' duration. No

jaundice, nausea or other symptoms were noted. Seven and a half years previously, however, he had an attack of right upper abdominal pain followed by jaundice. This was thought to be due to acute hepatitis. On examination, he had a rounded, exquisitely tender, right-upper-quadrant mass and ran a slightly elevated temperature (average 100.5°F.). He had a moderate anemia (hemoglobin 63 per cent), and white-cell counts ranged from 7000 to 10,000. He was thought possibly to have either a hydrops of the gall bladder or a cancer. However, an entirely normal cholecystogram was obtained.

In this case, the peritoneoscope was introduced in the left upper quadrant. The inferior surface of the liver was entirely normal. Numerous inflammatory adhesions in the right upper abdomen formed a curtain between the abdominal wall and the inner edge of the liver, and a large mass of omentum was densely adherent to the abdominal wall. Pericholecystic abscess seemed the likeliest diagnosis, yet could hardly have been present, since the Graham test was normal. An operation was performed, and a necrotic inflammatory mass was found in the omentum. Its origin was undetermined but thought possibly to be the result of a pancreatitis.

Here again, short of exploratory laparotomy, no diagnosis was possible other than by the means of peritoneoscopy. However, in this case a laparotomy was eventually needed.

#### GENERAL CONSIDERATIONS

##### *Carcinoma of the Stomach*

Some writers believe that every case of carcinoma of the stomach should be examined by peritoneoscopy before operation to determine the presence or absence of peritoneal and liver metastasis. If a palliative operation is indicated in any case, I consider peritoneoscopy unnecessary. Moreover, the operability in relation to posterior fixation and retroperitoneal metastases cannot be determined by peritoneoscopy. However, it is true that a small growth may already have hepatic metastases, whereas a large growth may have none and yet be quite operable. Peritoneoscopy may give strong evidence for either of these situations.

CASE 3. A. N. (F. H. 57649), a 62-year-old man, entered the hospital complaining of weakness, epigastric distress and evening anorexia of 2 weeks' duration. There was no nausea or vomiting, and a loss of only 6 pounds in weight. X-ray study showed a small carcinoma in the antrum of the stomach. Peritoneoscopy disclosed some confluent yellow masses in the left lobe of the liver typical of metastatic tumor, and a biopsy was obtained. No operation was performed, and the patient died 4 months later.

This man had a small carcinoma, with a short duration of symptoms, yet peritoneoscopy disclosed liver metastases. He later died without developing symptoms that surgery could have alleviated.

CASE 4. L. S. (F. H. 56330), a 63-year-old carpenter, complained of weakness, weight loss and tarry stools of 10 months' duration. The patient was emaciated. A large mass was palpable in the epigastrium. X-ray examina-

tion showed a large filling defect of the antrum of the stomach. Peritoneoscopy readily visualized the liver, and no metastases were present. No metastases were seen on the peritoneum, and the tumor did not appear to have come through the gastric surface. The patient was operated on, and an extensive resection performed after which he did well.

In contrast to the patient in Case 3, this man had a large growth of considerable duration. Symptoms were compatible with the presence of metastases. Peritoneoscopy gave encouragement to preparation for an extensive resection, which was carried out successfully.

### *Tumors of the Female Pelvic Organs*

In the majority of women, peritoneoscopies have been performed for the purpose of confirming by biopsy a strongly suspected diagnosis of ovarian

since no pelvic tumor could be felt. The diagnosis of a radiosensitive pelvic neoplasm was established.

**CASE 6** Mrs J R (F H 57461), a 43-year-old housewife had complained for 3 months, of an intermittent dull pain in the left flank. The catamenia were normal, and no genitourinary or gastrointestinal symptoms were noted. Examination showed an enormously obese woman with an overhanging panniculus of abdominal fat. An indefinite mass was at times felt high in the left pelvis. Abdominal x-ray examination was negative.

Peritoneoscopy showed a 10-cm ovarian cyst with a partial clockwise twist in its pedicle, but with no impairment of its blood supply. The other pelvic organs were normal.

The presence of an abdominal tumor was confirmed, and its nature determined, in an extremely obese woman in whom the very existence of the tumor was in some doubt.

### *Jaundice and Liver Diseases*

Peritoneoscopy is of greatest help in patients with jaundice and liver disease. A direct visualization of the liver and, if necessary, a biopsy give a far more accurate diagnosis than one based on clinical history and tests of liver function. The picture of cirrhosis, in contrast to the normal smooth liver surface, is as clear through the peritoneoscope as it is in the post mortem room. In cases of icterus without jaundice, and cases of intermittent jaundice with or without pain, the peritoneoscope will rule cirrhosis in or out. If a laparotomy must follow, to examine the pancreas or bile ducts, it will be performed with the conviction of its urgent need.

**CASE 7** R M (J H P D H 5143), a 59-year-old plumber, had felt weak and had tired easily for 14 months. Twelve months before entry slight jaundice had appeared and he consulted a clinic. All studies including a gastrointestinal series were negative. The degree of jaundice varied during the ensuing year; at times there was none. A medical consultant believed that statistically there was a 70 per cent chance that the trouble was due entirely to cirrhosis.

Peritoneoscopy showed an absolutely smooth liver surface and a greatly enlarged gall bladder fundus. This was considered strongly suggestive of an obstructing lesion of the lower biliary ducts.

A subsequent barium meal showed some narrowing of the second portion of the duodenum. At operation a carcinoma of the head of the pancreas was found.

### *SUMMARY AND CONCLUSIONS*

Peritoneoscopy has been safely performed in 75 cases. The gross pathologic lesions were identical

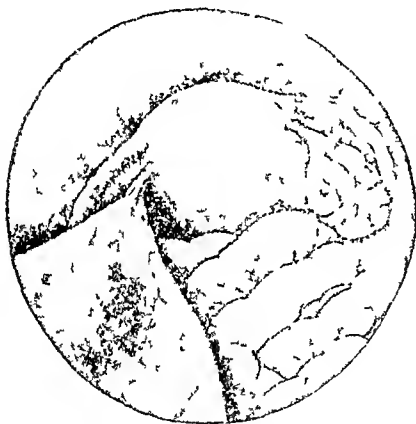


FIGURE 1 Ovarian Cyst and Female Pelvis as Seen through the Peritoneoscope (Case 6)

carcinoma. Some of the patients had ascites, and in 2 cases the pelvic tumors were not palpable from below, the peritoneoscope was consequently the only method of making a diagnosis and enabling x-ray treatment to be started.

**CASE 5** Mrs M D (F H 13161), a 49-year-old housewife entered the hospital complaining of a swollen abdomen of 7 months' duration. Examination showed some evidence of weight loss. No pelvic masses were felt. Repeated abdominal taps failed to give a diagnosis on spun sediment. Peritoneoscopy showed a nodular mass typical of ovarian tumor involving the left broad ligament and a biopsy showed a papillary adenocarcinoma.

Cirrhosis of the liver was considered in this case,

fied and a correct diagnosis returned in 55 cases. In 2 cases, both complicated by adhesions, it was impossible to be certain of the diagnosis. Fifteen biopsies were performed, all of which showed either a malignant tumor or a diseased liver. In

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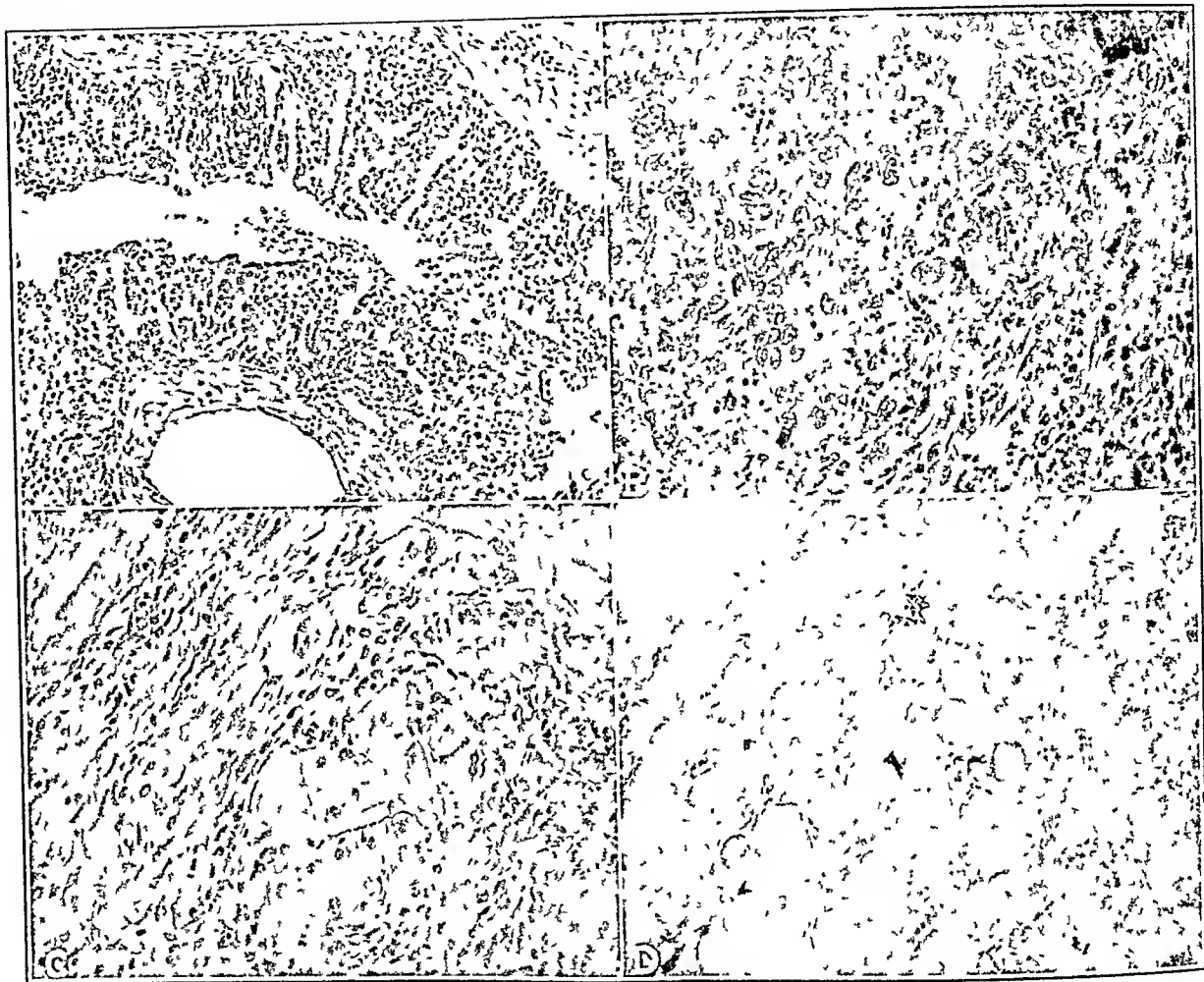


FIGURE 2. Biopsy Specimens Obtained through the Peritoneoscope.

A — carcinoma of the ovary; B — metastatic carcinoma of the liver, C — cirrhosis of the liver, D — fatty degeneration of the liver.

25 per cent of these cases, the findings fundamentally altered the treatment. In the remainder, accurate confirmation of a suspected diagnosis was obtained.

Peritoneoscopy is not merely useful: it is essential to the study of abdominal tumors and liver disease if needless laparotomies are to be avoided. It involves only a fraction of the expense or morbidity of a major operation.

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## MYOMECTOMY DURING PREGNANCY\*

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**A**LTHOUGH fibroids frequently coexist with pregnancy, they rarely cause serious complications. Pierson<sup>1</sup> found only 191 cases, or 0.6 per cent, of clinically important fibromyoma in 30,836 consecutive pregnancies analyzed at the Sloane Hospital for Women.

The uterus is usually very tolerant of the presence of fibroids, and I have observed many women with large tumors who progressed without difficulty through pregnancy, labor and the puerperium. The large growths are more frequently seen in elderly primiparas or in multiparas whose last baby was born several years previously. Fibroids that are palpated low on the uterine wall early in pregnancy may, as the uterus enlarges, be retracted out of the pelvis so that they offer no obstruction to labor. Intraligamentary and cervical fibroids usually do remain pelvic, however, and may necessitate abdominal delivery.

The occurrence of spontaneous abortion and premature labor is high. Pierson found it in 24.1 per cent of his series. Torsion of the pedicle may occur. A fibroid in the posterior wall may prevent replacement of a retroverted or retroflexed uterus. In 1930, I reported the suspension of an incarcerated, two-months-pregnant uterus with a large fibroid on the posterior wall. All attempts at replacement by conservative methods had failed, and miscarriage seemed imminent. The patient was delivered at term, and a myomectomy was performed four months later.

The chief complication during the prenatal period, however, is degeneration, the commonest type of which is so-called "red degeneration." This may occur with or without secondary hemorrhage in the tumor and is always associated with pain. The morbid process does not as a rule progress to actual death of the cells, but in neglected cases liquefaction and necrosis may ensue. Following this, the aseptic devitalized tissue may become infected through the blood stream or by contiguity from adherent intestine. The exact cause of this degeneration is not known, but it is believed to result from an interference with the blood supply of the fibroid by changes occurring in the pregnant uterus. This would explain why degeneration of these tumors is commoner dur-

ing the puerperium. The post partum administration of ergot should be withheld in these patients unless subinvolution or excessive flowing makes its use imperative.

Clinically, the onset of degenerative changes in the tumor is marked by pain, usually severe, over the site of the growth. An elevation of temperature of one or two degrees is usually noted, accompanied by moderate leukocytosis. Vaginal bleeding may or may not occur. In mild cases, the symptoms subside under rest and sedatives to control the pain. Conservative treatment should be given a thorough trial, but if the pain increases and the temperature and leukocyte count indicate that the degeneration is progressing unfavorably, surgery should be considered.

A report of 4 cases in which the fibroid was enucleated during pregnancy is presented.

## CASE REPORTS

**CASE 1.** Mrs. T., a 38 year-old woman, had been married 9 years and had never been pregnant. Her last regular period began on May 12, 1930. She flowed moderately from July 7 to 9 and then stained for 3 weeks. There was no pain or cramps, and she did not pass clots.

The patient had had no serious illnesses since childhood but a herniotomy and hemorrhoidectomy had been performed 12 years previously.

On September 3, she developed severe pain in the left lower quadrant and began to flow moderately. On examination, the abdomen was relaxed, and a tender mass could be felt in the left lower quadrant. Vaginal examination revealed a primiparous introitus, with a slight bloody discharge. The fundus was in good anterior position and was enlarged to a size consistent with a 3 months pregnancy. A firm, very tender mass, apparently attached to the uterus, could be felt in the left vault.

The temperature was 99.8°F, the pulse 96 and the respirations 22. The white-cell count was 12,500. The patient was admitted to the Trumbull Hospital. The following day, the pain had increased in severity, the temperature was 100°F, the pulse 98. The vaginal flowing persisted. On September 8 the white-cell count had risen to 16,000. The flowing increased, and two large clots were passed. The pain in the left lower quadrant became severe and could not be entirely controlled by sedatives. Laparotomy on that date revealed a uterus the size of a 3 months pregnancy, with a mottled, congested, apple-sized fibroid on the left anterior wall. Myomectomy was performed. Pathological examination of the tumor revealed red degeneration with marked small round-cell and polymorphonuclear infiltration. The following day, the patient was free from pain, and on the 3rd postoperative day the vaginal bleeding stopped and did not recur. Recovery was uneventful and pregnancy progressed normally until March 14, 1931. On that date, the membranes ruptured at 3 a.m. and the patient

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was admitted to the Massachusetts Women's Hospital. After 8 hours of ineffectual labor, a diagnosis of cephalopelvic disproportion was made, and a transverse cervical cesarean section was performed. On inspection, the myomectomy scar was found to be firm. A normal 10-pound, 4-ounce, baby was delivered, and after a normal convalescence the patient left the hospital on the 14th day.

CASE 2. Mrs. M., a 34-year-old woman, was seen in consultation at St. Margaret's Hospital on July 3, 1930. She had had two full-term normal deliveries, the last 5 years previously. Both children were living and well, and there had been no miscarriages. There had been no serious illness and no operations. The last regular period began on April 10, but there had been some irregular flowing off and on since that date and the patient did not believe that she was pregnant. On July 2, a laparotomy had been performed, and the uterus was found to be enlarged to a size consistent with a 2½ months' pregnancy. It was soft and blue, with a fibroid the size of a baseball growing from the fundus. A myomectomy was performed. When I saw the patient the following day, there was a slight bloody vaginal discharge, which ceased after 3 days. On July 12, vaginal examination revealed a uterus the size of a 3 months' pregnancy, with the fundus in good anterior position.

No further flowing occurred, and pregnancy proceeded normally to January 14, 1931. On that date, the patient was awakened at 5 a.m. by labor pains recurring every 5 minutes. She was admitted to St. Margaret's Hospital at 5:46 a.m. and delivered precipitately 6 minutes later. The normal infant weighed 7 pounds, 8 ounces, and the mother made an uneventful recovery.

CASE 3. Mrs. M., a 35-year-old woman, had been married 6 years. She had had no children or miscarriages. Her chief complaint was severe pain in the right lower quadrant of 2 days' duration. The last regular period began on June 27, 1931. On October 2, there had been a slight show of blood, with slight pain in the right lower quadrant. Two days later, the flowing increased, the pain became severer, and the patient was admitted to the Carney Hospital.

An attack of rheumatic fever, which did not affect the heart, was experienced in 1922. This was followed by a tonsillectomy, and there had been no recurrence. A hemorrhoidectomy had been performed 1 year previously.

On examination, there was marked tenderness in the right lower quadrant, and an indefinite mass could be felt, apparently attached to the uterus. There was no muscular spasm. On vaginal examination, the fundus was found to be enlarged to the size of a 3 months' pregnancy and was in good anterior position. There was a slight, steady, bloody vaginal discharge. On admission the temperature was 100.2°F., the pulse 94, the respirations 20, and the leukocyte count 12,000. The following day the flow increased, the temperature rose to 101.4°F., and the pain became severer.

On October 6, there was a steady bright-red vaginal flow, and the mass in the right lower quadrant was exquisitely tender. The white-cell count had risen to 15,600. Laparotomy revealed a uterus the size of a 3½ months' pregnancy, with a mottled, egg-sized fibroid protruding from the right anterior wall. A fibroid about half that size was seen on the left anterior surface of the uterus near the bladder reflection. The larger fibroid was enucleated. It extended well into the wall of the uterus, and a small area of amniotic sac could be seen

glistening in the depths of the uterine wound after the tumor had been removed. A few deep sutures were carefully placed, and the uterine incision closed. The smaller tumor was enucleated without difficulty. The patient made an uneventful recovery, and there was no vaginal bleeding after the 4th postoperative day.

Pregnancy progressed normally to term. On April 21, 1932, the patient was 2 weeks overdue. Because of cephalopelvic disproportion, on April 22, the patient was delivered by transverse cesarean section. The baby weighed 9 pounds, 6 ounces. The myomectomy scars were inspected and found to be firm. The patient made an uneventful recovery and was discharged 2 weeks later.

CASE 4. Mrs. C., a 39-year-old primipara, was seen in consultation with Dr. Chester Goodnow, of Franklin, Massachusetts, on October 31, 1939. Her last period began on March 21, and the expected date of confinement was December 28. For the previous month, the patient had had increasing discomfort and pain in the right flank. For 2 weeks, the pain had been so severe that the patient was unable to sleep. There had been no nausea or vomiting, and no flowing of blood since the last period.

The patient had always been well since childhood, and there had been no operations.

On examination, the fundus was found to be 4 finger-breadths below the ensiform; the fetal heart was heard in the left lower quadrant, and the rate was 144. A tender mass the size of an orange, apparently attached to the uterus but freely movable, could be felt about 8 cm. above the anterosuperior spine of the ilium. The tumor was exquisitely tender. The temperature, pulse and respirations were normal. The blood pressure was 136/84, and urinalysis was negative. On vaginal examination, the cervix could be palpated high in the vagina, and there were no pelvic masses or tenderness. The patient was anxious to have a normal, full-term baby, but said that she could not stand the pain any longer and requested that something be done.

The patient was admitted to the Milford Hospital on November 2. On the following day, laparotomy revealed a mottled, congested, pedunculated fibroid. A myomectomy was performed. An ampule of Progestin was administered daily for 4 days, and then twice a week for the next 2 weeks. Capsules of wheat-germ oil were also prescribed for a period of 4 weeks.

Pregnancy progressed without further incident, and the patient entered the Milford Hospital in labor on December 30. A normal, 7-pound, 4-ounce baby was delivered by low forceps by Dr. Goodnow. The post-partum period was uneventful, and the patient was discharged on the 13th day.

#### SUMMARY AND CONCLUSIONS

Fibroid tumors of the uterus usually have no harmful effect on a coexisting pregnancy.

The patient should be kept under careful observation for complications such as miscarriage or premature labor, obstruction to the descent of the presenting part and degeneration of the fibroid.

So-called "red degeneration" of the tumor is the type usually found, and it occurs most frequently during the puerperium, probably because involution disturbs its blood supply. Degeneration may also occur during the prenatal period. Its onset is

always marked by pain, occasionally accompanied by fever and leukocytosis.

When the degeneration is slight, the symptoms may be relieved by medical treatment, but in the severer types the tumor should be removed. Interruption of the pregnancy should not result from the operation. On the contrary, myomectomy seems to prevent miscarriage.

Corpus luteum hormone and wheat-germ oil

should be administered prophylactically, whether the fibroid is treated conservatively or removed.

Four cases of myomectomy during pregnancy, with delivery at term, are presented.

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## MEDICAL PROGRESS

### CHEMOTHERAPY OF PNEUMONIA\*

With Special Reference to the Present Status of Sulfadiazine

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ANY review of recent progress in the treatment of pneumonia must concern itself primarily with chemotherapy. New developments continue to take place rapidly in this field. Lord's<sup>1</sup> summary in 1939 covered the introduction of sulfonamide drugs in the treatment of pneumococcal pneumonias. He concluded that sulfanilamide, the first important chemical of the group to be widely used in this country, although it had some value in the treatment of pneumonia was less effective and likelier to produce toxic effects than sulfapyridine. The latter had already received quite extensive clinical trial at that time, and the favorable results of its use were fully corroborated in many further reports<sup>2</sup> collected from the literature during the following year.

#### RESULTS OF SULFATHIAZOLE THERAPY

Sulfathiazole made its appearance shortly before the last review.<sup>2</sup> The preliminary clinical observations at that time indicated that this drug was less toxic than sulfapyridine, particularly with respect to nausea and vomiting, which were the most frequent and very disturbing features of sulfapyridine therapy. The two drugs appeared to be about equally effective in the treatment of the pneumococcal pneumonias.

#### Mortality

Numerous reports dealing with sulfathiazole therapy have appeared during the past year. The pneumonias in adults treated with this drug by a

number of different authors<sup>3-10</sup> include 1045 cases of pneumococcal pneumonia, with 98 deaths, a mortality of 9.4 per cent. These cases also include patients (about 9 per cent of the total) who received serum in addition to sulfathiazole, usually because of inadequate response to the drug. Also included are cases treated with sulfamethylthiazole, which was found to have a very similar action but which, owing to the development of occasional cases of peripheral-nerve lesions and even encephalopathy<sup>16, 17</sup> resulting from its use, was subsequently withdrawn from further clinical trial. A few authors<sup>7-9</sup> have also included comparable and contemporaneous cases from the same clinics treated with sulfapyridine, alone or with serum, both used in about the same manner as in the sulfathiazole-treated cases. There were 1501 such sulfapyridine-treated cases, with 204 deaths, a mortality of 13.7 per cent. Bacteremia was just as frequent in either group, — 15.2 and 15.3 per cent in the patients treated with sulfathiazole and sulfapyridine, respectively, — but the mortality in these bacteremic cases was 25.2 per cent among the former as compared with 32.6 per cent in the latter.

In general, individual reports have indicated that the effect on mortality and on the clinical course in adults was about the same or slightly better with sulfathiazole as compared with sulfapyridine. Some writers<sup>6, 8</sup> have noted a more rapid defervescence in sulfapyridine-treated cases, but this may have been due, at least in part, to the antipyretic effect of this drug, which either is lacking or is less apparent with sulfathiazole.<sup>18</sup>

#### Results in Children

In the pneumonias of infants and children, also, the effects of these two drugs have been very similar.<sup>19-21</sup> In the largest series,<sup>22</sup> the mortality

\*All articles in this series will be published in book form: the current volume is *Medical Progress Annual 1940* (Springfield, Illinois: Charles C. Thomas Company, 1941, \$4.00).

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was 4 per cent in patients under the age of two years and 2 per cent in those over two years. Patients who were moribund on admission and died within twenty-four hours of entry to the hospital were also included. The latter cases accounted for about half the fatalities. The average duration of fever was almost exactly the same with the two drugs.

### *Toxicity*

Sulfathiazole has proved simpler to administer than sulfapyridine, solely because it produces nausea and vomiting less frequently. Among adults, this effect is observed in 20 to 40 per cent of sulfathiazole recipients, as compared with 60 per cent or more of those who receive sulfapyridine. It is noted much less frequently in infants and children treated with either drug. Furthermore, the severity of this symptom is considerably less when sulfathiazole is used, so that therapy must be discontinued or interrupted less frequently. This may be the explanation for the lower incidence of relapses of fever and of pulmonary signs and symptoms after sulfathiazole therapy is discontinued, as compared with the incidence of these complications with sulfapyridine treatment. It may also account for the larger average amounts of drug used in the sulfathiazole-treated pneumonias. The larger dosage, however, may also be explained, in part, by the lower blood levels obtained when sulfathiazole is used in the same doses as sulfapyridine. Some physicians are consequently inclined to increase the dose of sulfathiazole in an attempt to obtain higher levels.

Sulfathiazole also has the advantage of not producing cyanosis or anemia, and it produces serious leukopenia and liver damage less often than sulfapyridine. On the other hand, drug fevers and rashes occur much more frequently with sulfathiazole. The characteristic lesions, which resemble erythema nodosum, on the extensor surfaces of the extremities, in addition to the episcleritis and the erysipeloid lesions of the face and the severe arthritis that sometimes accompanies the skin manifestations, are features of sulfathiazole toxicity not met with in sulfapyridine-treated cases.

### *Renal Symptoms*

The most important toxic effects of sulfathiazole therapy, however, are the renal complications, which are encountered at least as frequently and probably oftener than with sulfapyridine and may be considerably more serious.<sup>22-30</sup> The increased danger from the renal complications of sulfathiazole therapy is related to the tendency

of this chemical to precipitate, in both the free and the acetylated form, in the tubules of the kidneys, and thus to interfere with renal function either mechanically or by a direct action on the tubular epithelium. This mechanism may be operative in sulfapyridine-treated cases,<sup>31</sup> but is not the usual mechanism with that drug. It may account for some failures to obtain relief of sulfathiazole anuria by catheterization of the ureters and lavage of the kidney pelvis and of the ureters, a method that is often successful if applied early in the anuria caused by sulfapyridine.<sup>32-36</sup> With sulfapyridine, the concretions of the acetylated drug are usually limited to the kidney pelvis, the ureters and the bladder. Reduced renal function in the course of continuous sulfathiazole therapy is not infrequent in animals and in clinical cases, but the function usually returns to normal after the drug is discontinued.

Because of the frequency and possible severity of the renal complications, it is essential to be on the alert for the earliest evidence of kidney damage in every patient who is treated with sulfathiazole. The urinary output must be maintained at about 1500 cc. or more daily (in adults), and the fluid intake should be adjusted accordingly. Usually, an intake of about 3000 cc. a day is necessary. Diminution in urinary output, the appearance of hematuria, retention of the drug in the blood or elevation of the blood nonprotein nitrogen is a danger sign. When one of these manifestations occurs, the drug must be stopped or the dose reduced, and the fluid intake increased. Intravenous or subcutaneous fluid in the form of physiologic saline or of 0.5 per cent glucose in water may well be used at first. Alkalies may also be helpful, and may be given as bicarbonate of soda by mouth or as a one-sixth molar solution of sodium lactate intravenously.

### TREND IN PNEUMONIA MORTALITY

Mention was made last year of the trend in mortality since the introduction of effective sulfonamides.<sup>2, 37</sup> The gross mortality for the country as a whole is difficult to evaluate because of many factors involved in the collection of such data. Some of the clinical reports, however, seem to indicate a rising case-fatality rate in chemically treated cases, even when the same drug is employed. Thus the mortality among adults in Lord's<sup>1</sup> collected cases treated with sulfapyridine was 6.3 per cent. Among the cases collected during the following year, the mortality was 9.8 per cent,<sup>2</sup> and, as noted above, the mortality was 13.7 per cent in sulfapyridine-treated cases reported during the past year by a number of workers. To

be sure, the data for the successive years are not strictly comparable, but a similar rise in the case-fatality rate has been noted in more selected groups, as, for example, in the pneumococcal pneumonias reported by a group of workers in Philadelphia. In their earliest experience with sulfapyridine, they<sup>38</sup> reported a mortality of 70 per cent in 400 cases. During the following year, they recorded a mortality of 150 per cent in 200 cases treated with the same drug. In that year, they had a mortality of 110 per cent in a parallel series of 200 cases treated with sulfathiazole. Early last season, the same group<sup>14</sup> reported two parallel series, each consisting of 100 cases of pneumonia, one series treated with sulfathiazole, with 17 deaths, and the other treated with sulfadiazine, with 11 deaths. If only the "typed" pneumococcal pneumonias are considered, as in their previous studies, the mortality in the sulfathiazole treated cases was 19 per cent and in the sulfadiazine cases it was 13 per cent.<sup>13</sup>

A number of possible explanations of this trend may be mentioned. The first is that the severity of the disease has increased. The slight increase in the incidence of bacteremia, with the rising mortality, lends some support to this view. An increase in the occurrence of "drug resistant" strains might account for more failures of drug therapy, but this has been proved only in rare cases. It is possible that, as the early enthusiasm accompanying a new clinical therapeutic venture wore off, stricter criteria were used in the choice of cases for inclusion in succeeding studies. This explanation likewise seems inadequate, since, if anything, the general trend has been in the opposite direction and more cases are being included for chemotherapy as experience with the drugs increases. It seems likelier that in most communities, as acquaintance with the sulfonamides diffuses among physicians, greater numbers of cases are treated by them in the home. Only the severer cases and those offering difficulties in management are sent to the clinics from which the reports emanate. Thus, in a large municipal hospital receiving primarily indigent patients, few of whom could afford treatment by private physicians, the mortality in all specifically treated cases has actually dropped in the last three successive years.<sup>7, 39, 40</sup>

That chemotherapy may be used successfully in the home in the great majority of cases, even among indigent patients, is shown strikingly by the work of the group of physicians at the Boston Dispensary, who are interested in domiciliary medicine.<sup>41</sup> Because most cases are successfully treated in the home, it is to be expected that hos-

pital clinics and physicians engaged exclusively in consultation practice will have a higher mortality in their pneumonia cases than the internist or general practitioner in private practice.<sup>42</sup>

#### SULFADIAZINE

Of the more recent sulfonamide compounds, the one that has received the most extensive trials during the past season is sulfadiazine. This chemical, which was prepared by Roblin and his associates,<sup>43</sup> is the pyrimidine (diazine) analog of sulfapyridine and sulfathiazole. A preliminary report concerning this drug was made by Long<sup>44</sup> for the Council on Pharmacy and Chemistry of the American Medical Association, and the laboratory and clinical results obtained at the Boston City Hospital have also been published recently.<sup>10</sup> Although these two papers summarize most of the relevant data about sulfadiazine that are available at the time of this writing, the drug has proved to be of sufficient interest in relation to the treatment of pneumonia and other infections to warrant the inclusion here of a review of the more important information available concerning its use.

#### *Results in Animals*

Pharmacologic and therapeutic experiments with sulfadiazine were carried out in animals by Feinstein and his associates.<sup>45</sup> They found that this compound is less toxic than either sulfapyridine or sulfathiazole in acute experiments in mice, and that it produces less tissue damage than the latter drugs after prolonged administration in monkeys. They showed that sulfadiazine is absorbed fairly rapidly after oral administration, and that much higher levels are reached in the blood and are maintained longer than when the same doses of the other sulfonamides are used. Furthermore, the drug is found in the blood primarily in the free or unconjugated form. The acetyl derivative of sulfadiazine is excreted rapidly in the urine, where it is more soluble than the corresponding forms of sulfapyridine or sulfathiazole. Using identical dosage in mice, Feinstein found sulfadiazine to be more effective than either sulfapyridine or sulfathiazole against infections with hemolytic streptococcus, Type 1 pneumococcus and Type B Friedlander's bacillus, and about as effective as sulfathiazole against infections with staphylococcus.

Long<sup>44</sup> showed that in mice kept at the same blood levels, which can be maintained with considerably smaller doses of sulfadiazine than of the other sulfonamides, this drug is somewhat less effective than sulfanilamide against hemolytic

streptococcus and also slightly less effective than sulfapyridine or sulfathiazole in Type-1 pneumococcus infections, but is equal if not superior to sulfathiazole against staphylococcal infections. He also noted that sulfadiazine, when administered orally or locally, is more effective than sulfapyridine or sulfathiazole in experimental infections produced in mice by the intramuscular injection of *Clostridium welchii* and *Cl. oedematis maligni*, but that none of the drugs have any effect against *Cl. oedematis* infections. Klinefelter<sup>16</sup> found that sulfadiazine is also more effective than sulfathiazole against *Escherichia coli* infections in mice. He maintained approximately the same blood levels with about one tenth as much sulfadiazine.

### Results in Vitro

Studies on the effect of sulfadiazine on the growth of various bacteria in vitro<sup>40, 46-50</sup> have been inconsistent and somewhat misleading, since they have not always paralleled the effects observed in clinical and experimental infections. Against most of the organisms tested, it has been found to be about as effective as sulfathiazole, but against others it appears to be much less effective. The discrepancies may be accounted for by the methods used. In particular, they may be associated with differences in the mediums used for the tests, some of which may exert a selectively greater inhibiting effect on some drugs than on others. This has been shown to be true in test-tube experiments with pneumococcus.<sup>17</sup>

### Absorption and Excretion in Man

The absorption, excretion and distribution of sulfadiazine in human subjects with normal renal function have been studied by several workers.<sup>44, 51-54</sup> As in animals, higher concentrations are reached in the blood and are maintained for longer periods than with the same dose of any of the other commonly used sulfonamides, namely, sulfanilamide, sulfapyridine and sulfathiazole. Absorption from oral administration may be somewhat slower than with the latter compounds. Very little of the acetylated derivative is found in the blood. Up to 80 per cent of the ingested drug is excreted into the urine, and about one third of the drug recovered from this source is in the conjugated (acetylated) form. The drug diffuses rather slowly into the cerebrospinal fluid, requiring about eight to twelve hours to reach an equilibrium with the blood. On continuous therapy, the concentration in spinal fluid is usually about 80 per cent of the blood level, but may range from 50 to over 90 per cent. In pleural and ascitic fluids, the levels are essentially the same as in the

blood. Sulfadiazine, like sulfapyridine and sulfathiazole, is only very slightly absorbed after rectal administration, even when the sodium salt is used. Like sulfathiazole, and in contrast to sulfapyridine and sulfanilamide, sulfadiazine is found in much lower concentration in the red blood cells than in the surrounding plasma.

### Parenteral Administration

The sodium salt of sulfadiazine has been used parenterally in the same manner as the corresponding salt of sulfapyridine and sulfathiazole. It has been given intravenously as a 5 per cent solution in distilled water, or in concentrations of 0.5 to 2.0 per cent in physiologic saline solution, and has also been injected subcutaneously and intrathecally in 0.5 per cent solution in physiologic saline solution, without untoward effects.

### Clinical Results in Pneumonia and Other Infections

Published clinical data are still comparatively meager and, for the most part, are given only in preliminary form. In the two parallel series of 100 pneumonia cases referred to previously, the effectiveness of sulfadiazine compared favorably with that of sulfathiazole, with respect both to mortality and to the rapidity with which the temperature fell in the recovered cases.<sup>8</sup> Long,<sup>44</sup> in his early experience, found that "sulfadiazine is slightly less effective than sulfapyridine or sulfathiazole in the treatment of pneumococcal pneumonia in human beings and that it is of definite value in the treatment of hemolytic streptococcus and staphylococcal infections in man." Plummer<sup>55</sup> noted that, in a small series of pneumococcal pneumonias, the clinical results compared favorably with those obtained with sulfapyridine and sulfathiazole, and that in certain other infections, particularly those due to Friedländer's bacillus, the results were encouraging. In another paper, he<sup>9</sup> included 51 patients with pneumococcal pneumonia treated with sulfadiazine, with 9 deaths, or a mortality rate of 18 per cent, as compared with 69 deaths, or a rate of 12 per cent, among others treated with sulfapyridine, sulfathiazole or their congeners. Serum was used, in addition, in some of the cases treated with each of the drugs.

The 446 sulfadiazine-treated cases reported from the Boston City Hospital<sup>10</sup> included a variety of infections. Among them were 178 patients with pneumococcal pneumonia, of whom 19, or 11 per cent, died. This is the lowest mortality in any comparable group of cases previously reported from this clinic. The drug was also effective in pneumonias due to hemolytic streptococcus and

staphylococcus, in meningococcal infections, in acute infections of the upper respiratory tract, including sinusitis, in erysipelas, in acute urinary tract infections, particularly those due to the colon bacillus, and in acute gonococcal arthritis. So far as could be judged from the small numbers of cases, sulfadiazine appeared to be as effective as sulfapyridine or sulfathiazole in each of these conditions. Dingle, Thomas and Morton<sup>50</sup> also found sulfadiazine to be highly effective in the treatment of a small series of cases of meningococcal meningitis, including both the epidemic and the endemic forms.

### Toxic Effects

All the reports indicate that toxic manifestations from sulfadiazine are encountered much less frequently than with any of the other common sulfonamides. The toxic effects that were noted among the 872 cases reported by various authors<sup>10 44 53 55 56</sup> may be summarized briefly. Nausea and vomiting occurred in 94 per cent of the cases, dermatitis in 17 per cent, fever alone in 04 per cent, hematuria in 10 per cent, headache or vertigo in 06 per cent, and leukopenia in 18 per cent. Crystals were found in the urine in 117 per cent of the cases. The following manifestations were each mentioned by only one author and were not noted by the others: scleral and conjunctival injection was noted in 2 of Long's<sup>44</sup> 125 cases, and a questionable psychosis was noted in 7 of Flippin's<sup>15</sup> 100 cases. Nitrogen retention in the blood occurred in 11 per cent of our cases,<sup>40</sup> and one case of anuria, relieved by ureteral catheterization, was included. Another case of anuria, unrelieved by catheterization and ending fatally, has been observed more recently.

Long<sup>44</sup> has noted that, even in the face of grave kidney damage, the free and conjugated fractions of sulfadiazine seem to be more readily excreted by the damaged kidney than is usually the case with sulfapyridine and sulfathiazole, and this corresponds with our experience.<sup>40</sup> Anemia and cyanosis have not been observed in any of the cases. With respect to the cyanosis, it has been shown that carbonic anhydrase is not inhibited by sulfadiazine or by sulfathiazole, but it is inhibited by sulfanilamide, which caused this symptom so frequently.<sup>54</sup>

### Dosage

In general, sulfadiazine has been used in the same doses as the other sulfonamides. It is given orally whenever possible. The initial dose for adults is 4 gm, and this is followed by 1 gm every four hours until the temperature reaches normal; some prefer to continue this dose for one

or two days longer. It is then reduced to 1 gm. every six hours. Blood levels between 7 and 10 mg per 100 cc are maintained readily on this schedule in most patients who are on an adequate fluid intake (2500 to 3000 cc. daily). In patients who are comatose or vomiting severely, and in others who are extremely ill, it may be of advantage to give an initial dose of 5 gm of the sodium salt parenterally in the manner already mentioned. Follow up doses of 2 or 3 gm of the sodium salt may then be given at intervals of eight to twelve hours, preferably subcutaneously in 400 or 600 cc (0.5 per cent) of physiologic saline solution, but a shift to the oral route should be made as soon as possible.

### FAILURES AND SECONDARY FEVERS IN SULFONAMIDE-TREATED CASES OF PNEUMOCOCCAL PNEUMONIA

The factors influencing mortality have recently been analyzed in a group of 800 cases of adult pneumococcal pneumonia treated with sulfapyridine and sulfathiazole.<sup>50</sup> The most important factors were age and bacteremia. The mortality in the patients over forty years of age was 154 per cent, a rate almost four and a half times as great as that in those less than forty years old (35 per cent). The bacteremic patients had a mortality rate of 32.3 per cent, which was nearly five times as high as that in the patients with negative blood cultures (6.8 per cent). Late treatment was also an important factor. When treatment was started on the fifth day or later, the mortality (18.4 per cent) was almost three times as high as that in the patients in whom treatment was begun on the fourth day or earlier (5.6 per cent). The type of pneumococcus was also important. The death rate in the Type-3 cases was 20 per cent, as compared with 10.5 and 7.0 per cent in Type 1 and Type 2 cases, respectively, and 8.0 per cent in those due to other types. Complications of the pneumonia influenced the mortality appreciably, but much less than the presence of other associated severe diseases. The most frequent of the latter were heart disease and alcoholism. The mortality in the cardiac patients was 31.3 per cent, and among the alcoholics, 20.5 per cent. Sex and color had no appreciable effect on the mortality in these cases.

These findings are in essential agreement with the results of all other analyses of mortality in cases of pneumococcal pneumonia that have been recorded in the past. The same factors are equally important in patients treated symptomatically without the aid of specific measures, as well as in patients treated specifically with serums or chemicals, or both. It is not to be inferred, however, that old patients, those with bacteremia or with Type 3

pneumococcus infections and those with associated diseases, are not benefited by the therapy. The prognosis for recovery without specific treatment is very poor in such cases, but the reduction in death rate and the improvement in the clinical course resulting from chemotherapy are almost of the same order as among other cases.<sup>60</sup> This was clearly demonstrated recently for the old-age pneumonias. In one group of such cases, the mortality was reduced from an average of 75.0 per cent to 23.5 per cent by the use of sulfapyridine, and the average duration of fever was reduced from twelve to three days by chemotherapy.<sup>61</sup>

The causes of secondary fever among 339 sulfapyridine-treated cases of pneumococcal pneumonia were reviewed recently by Dowling and Abernethy.<sup>62</sup> Relapses of fever and symptoms of pneumonia occurred in 15 cases after apparent temporary improvement, but before the signs and symptoms had entirely cleared. In 7 of these cases, the dose seemed to be adequate, as judged by the high levels of the drug in the blood. Five of the cases, including 4 of the latter, were Type-3 pneumococcus pneumonias, and 3 of the 4 deaths among these 15 cases were in patients with this type. It is of interest in this connection that Type-3 strains have been found to respond less regularly to sulfapyridine therapy than Type-1 or Type-2 strains in experimental infections in mice.<sup>63</sup>

So-called "drug fever" occurred in 7 cases reported by Dowling and Abernethy. This diagnosis was based on the concomitant presence of a morbilliform rash in 3 cases, and on high fever, without signs of marked toxicity or in the absence of other demonstrable cause of fever, in the remaining cases. The drug fever began from two to four and one-half days after the crisis and continued for one and one-half to four days, regardless of whether administration of the drug was continued or stopped. All these patients recovered.

In 6 of Dowling and Abernethy's patients, a second attack of pneumonia caused by a different type of pneumococcus occurred while treatment with sulfapyridine was being continued and after apparent recovery from the original attack. All these patients recovered from the recurrence. Serum was used, in addition to sulfapyridine, in the first attack in 2 cases, and sulfapyridine was used alone in all the other attacks, except in 2 of the recurrences, in which only symptomatic treatment was given. Such recurrences have not been encountered previously by these authors in any of 65 patients who were treated symptomatically, and occurred in only 1 out of 120 cases treated with serum alone.

The fourth cause of secondary fever, according

to Dowling and Abernethy, was the occurrence of complications of the pneumonia. This accounted for 4 cases.

In the experiences with sulfathiazole referred to earlier, relapses and recurrences have been much less frequent than with sulfapyridine. On the other hand, drug fevers and rashes were considerably more frequent. Sulfathiazole fevers, with or without dermatitis, may be associated with severe symptoms, including chills, so that a relapse of infection or the occurrence of complications or of other intercurrent infections is suspected, but the pulmonary symptoms do not recur. It has been our experience that sulfathiazole fever, especially when accompanied by a rash, usually progresses under continued treatment and only rarely subsides before the drug is withdrawn.

#### CHEMOTHERAPY IN NONPNEUMOCOCCAL PNEUMONIAS

Most of the reports dealing with the chemotherapy of pneumonia and containing bacteriologic data have dealt primarily with pneumococcal pneumonias. Occasional cases of primary pneumonia due to other organisms are included. Sulfonamides have been used in such cases because of the known effectiveness of the drugs in other infections with the same organisms or because no other effective remedy is available. It is therefore difficult to assess the value of chemotherapy under such conditions. A few recent reports have dealt primarily with nonpneumococcal pneumonias and may be reviewed briefly.

##### *Streptococcal Pneumonia*

Lawrence and Sutliff<sup>64</sup> have recently summarized part of the experience of the New York City pneumonia-control program with respect to the role of hemolytic streptococci in pneumonia. During the winter of their study, 5.05 per cent of all sputum specimens examined in the health department laboratory yielded cultures in which more than 15 per cent of the colonies were hemolytic streptococci. In 15 of 141 patients from whom these specimens were obtained, there was no pneumonia. In 45 of the others, the streptococci were associated with pneumococci, and in the remaining 81 cases of pneumonia the streptococcus was the only significant organism.

The fatality rate for their entire series of 126 cases was 10.3 per cent. Only 22 of the cases were hospitalized, and 7 of the 13 patients who died were hospitalized. This makes a fatality rate of 6 per cent in the home-treated cases and 32 per cent in the hospitalized patients. Empyema occurred in only 3 per cent of all the cases and

in 18 per cent of those treated in hospitals. In 10 cases receiving adequate doses of sulfanilamide, there were no deaths; among 57 cases receiving less than the generally recommended doses of sulfanilamide, 8 deaths were reported, a fatality rate of 14 per cent; and of 59 patients who received no sulfanilamide, 4 died, a rate of 8 per cent.

Keefe, Rantz and Rammelkamp<sup>65</sup> studied 55 cases of hemolytic streptococcus pneumonia and empyema treated with sulfanilamide and sulfapyridine. There were 39 cases of pneumonia alone, and 14 of the other 16 cases had empyema, which followed an infection of the lung. The mortality rate in all the cases was 18 per cent, and it was the same whether or not empyema was present. Bacteremia occurred in 7 patients, of whom 4 died. In these cases, the use of sulfanilamide or sulfapyridine did not reduce the incidence of empyema, nor did it shorten the course of the disease. There was suggestive evidence that the fatality rate in both the cases of pneumonia and empyema was reduced by using these drugs. Four patients with empyema recovered following multiple aspirations of the chest, and chemotherapy. The best results, however, were obtained with a combination of chemotherapy and thoracotomy.

Carey<sup>20</sup> used sulfapyridine in the treatment of 42 infants and children with hemolytic streptococcus pneumonia, and also treated 21 such patients with sulfathiazole. The death rate in patients under two years of age was 26 per cent, and in those over two years old it was 6 per cent. After those who died within twenty-four hours were excluded, the death rate was 3 per cent in each group. There was no significant difference in the average duration of the disease after treatment with the two drugs used.

Sulfadiazine has proved highly effective in the few cases of hemolytic streptococcus pneumonia in adults in which it has been used.<sup>49, 40</sup> Of the 4 cases included in our report,<sup>40</sup> 2 had bacteremia and 2, including 1 of the latter, had empyema. All 4 patients recovered completely without operation.

### *Staphylococcal Pneumonia*

Although numerous reports are available of sulfonamide-treated cases of staphylococcal infections, particularly cases of staphylococcal sepsis treated with sulfathiazole, data concerning the effects of the drugs in primary pneumonias due to *Staphylococcus aureus* are very scant. Individual cases or groups of a few such cases are scattered among some of the reports dealing with the chemotherapy of pneumonia or of staphylococ-

cal infections. On the whole, the results of treatment with sulfanilamide or sulfapyridine have not been favorable except, perhaps, in individual cases. On the other hand, the results of sulfathiazole therapy have been encouraging.

Carey<sup>20</sup> included 15 cases of staphylococcal pneumonia in his series. The fatality rate was 50 per cent in infants under two years of age, if the patients dying within twenty-four hours of admission to the hospital are included. Sulfapyridine was used in 8 of the patients, all of whom died, whereas 5 of the 7 sulfathiazole-treated patients recovered. One of the sulfathiazole-treated patients died ten hours after entry to the hospital, whereas the other died after seven days of intensive treatment with this drug. Shulman<sup>66</sup> has recently reported 2 severe cases of staphylococcal tracheobronchitis in infants successfully treated with sulfamethylthiazole and sulfathiazole.

Our report on sulfadiazine therapy<sup>40</sup> included 29 cases of staphylococcal pneumonia. Positive blood cultures for *Staph aureus* were obtained from 3 of the patients, all of whom recovered. In addition to the staphylococcus, influenza bacilli were cultivated from 3 cases and hemolytic streptococci from 5, including a patient in whom the latter organism invaded the blood stream. There were 6 deaths (21 per cent) among the 29 cases, including the one with hemolytic streptococcus bacteremia. Fluid was obtained by thoracentesis in 6 of the patients who recovered. The original fluid and subsequent ones were all sterile in 2 of these cases. In the remaining 4, the original fluid was infected with staphylococci; 2 of these patients recovered completely following sulfadiazine therapy and thoracenteses, and the other 2 were drained by thoracotomy. A number of cases of staphylococcal pneumonia occurred during the past winter as complications of epidemic influenza, which was prevalent at that time. Except for some fulminating cases, these patients responded well to either sulfathiazole or sulfadiazine, although the course was frequently prolonged or associated with empyema or with abscess formation in the lungs.<sup>67</sup>

### *Friedlander Pneumonia*

The mortality in acute primary Friedlander pneumonia treated without specific agents is very high. Only 1 patient in 32 cases reported by Solomon<sup>68</sup> recovered, and all of 5 treated with serum died. In Bullowa's<sup>69</sup> first series, there were 7 recoveries among 41 cases, a mortality of 83 per cent. Among the 24 cases in his series that were due to the Type A Friedlander bacillus, 6 patients received type-specific serum, and 3 recov-

ered, whereas only 1 recovered among the 18 who were treated without specific serum. More recently, Solomon<sup>70</sup> reported a group of 17 cases of chronic Friedländer bacillus pneumonia. Sulfapyridine was used in 4 of these patients, all of whom recovered, although pulmonary suppuration continued without apparent effect. One of these patients had a positive blood culture. Another bacteremic patient was treated with sulfanilamide and recovered, although he, too, contracted lung abscesses. Among the 12 patients treated without sulfonamide drugs, there were 4 deaths, but 2 of those who recovered had positive blood cultures. More recently, Perlman and Bullowa<sup>71</sup> presented a second series of 37 cases of primary Friedländer pneumonia, with a mortality of 84 per cent. Among these patients, 9 were treated with sulfanilamide or sulfapyridine, and 6 died; 7 received these sulfonamides in addition to specific serum, and only 1 recovered; 13 with Type-A infection received specific serum alone, and all died; and of 8 who were given only symptomatic treatment, 2 recovered.

These reports indicate that treatment with sulfanilamide or sulfapyridine may be successful in individual cases, but the results as a whole are not very favorable. Reports of sulfathiazole-treated cases are still too few to evaluate. However, the greater effectiveness of sulfadiazine in experimental Friedländer-bacillus infections<sup>45</sup> suggests that one may look forward to better results from this drug.

### *Pneumonias of Undetermined Etiology*

Recent reports concerning chemotherapy in pneumonia include a considerable number of cases in which the bacteriologic studies fail to yield pneumococci or other organisms that might be considered etiologic. In many of these cases, the predominant organism obtained from direct cultures of the sputum is either *Streptococcus viridans* or a nonhemolytic or slightly hemolytic (alpha) streptococcus. The relation of such streptococci to the disease is difficult to evaluate, although in rare cases they seem to be significant, since they are also obtained in cultures of the blood or of pleural exudate and are frequently cultivated from the lungs at autopsy. Some of these cases have all the clinical features of typical lobar pneumonia, whereas others have atypical lesions and symptoms. Most of these patients apparently respond well to sulfonamides. Among 52 cases treated with sulfadiazine, there were 3 deaths, and all the fatal cases were in patients over sixty years old who had atypical pneumonias.<sup>40</sup> It is possible that many of the cases in this category,

particularly those with typical lobar pneumonia that respond so well to chemotherapy, are cases of mild pneumococcal pneumonia in which the causative organism escapes detection. Other cases of atypical pneumonia in which the patients fail to show any clinical response but nevertheless eventually recover may be due to viruses as yet unidentified.

Attention was called recently to a group of atypical pulmonary infections complicating severe and intractable bronchial asthma or congestive cardiac failure. The bacteriology in these cases is often unrevealing. Proper treatment of these cases with sulfathiazole or sulfadiazine may not only result in prompt improvement in the pulmonary infection, but may also render the underlying condition more amenable to appropriate treatment.<sup>72</sup>

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 27311

#### PRESENTATION OF CASE

A thirty-year-old housewife entered the hospital complaining of generalized aches and pains.

The patient felt well until five years before admission, when a rather severe, sharp pain developed in her left knee; this was aggravated by motion. Six months later, a tender swelling appeared above this joint; and the pain extended to her left hip and lower back, and another swelling developed in the right tibia. Approximately one year after the onset of her symptoms, several bone cysts were said to have been removed from her jaw. Three years before entry, and without untoward symptoms, the patient gave birth to a normal child by forceps delivery; during her confinement she suffered from severe pyorrhea. Shortly afterward, the back pain became severer and spread to the thoracic spine, sternum, left shoulder and lower left ribs, where another tender swelling developed. At that time the patient entered an outside hospital, where her complaints were generalized aches and pains, polyuria and polydipsia. Examination revealed bilateral exophthalmos and small painless swellings over the mandible and tibia. X-ray study showed areas of decreased density in the skull and jaws, with a large cystic growth in the right tibia. An intravenous pyelogram demonstrated a calculus in the left ureter, with no dye from the right kidney. The blood calcium was 13 mg., the phosphorus 2.8 mg. per 100 cc. and the basal metabolic rate +9 per cent. A bilateral cervical exploration for a parathyroid tumor was performed without success. Two weeks later, an air injection into the mediastinum revealed no tumor, and subsequent exploration of the anterior mediastinum was fruitless. The patient was discharged from the hospital for a rest period, with a view to re-exploration. Several weeks later, however, she visited her own physician and complained of nervousness. A thyroidectomy was thereupon performed, but the apparent benefit derived from this procedure was short lived and her aches and pains returned, with pronounced tenderness over the tumor sites.

During the period between two years and one

year before admission, the patient suffered from severe headaches, most marked in the right temporal region, with tenderness in the entire calvarium; and for the previous eight months she had been forced to remain in bed, not from weakness, but because of pain.

Six months before admission, the patient entered a clinic, where another parathyroid exploration was unsuccessful.

At the time of admission to this hospital, in addition to her other symptoms, she complained of chest pain aggravated by deep breathing and coughing. There had been no loss in weight. A frequency of urination, with a nocturia of one to three times, had been present for about five years.

The family history was irrelevant. The patient had had the usual childhood diseases. She was in the habit of drinking a quart of milk each day.

On examination, the patient exhibited a yellowish pallor and was chronically ill, but in no obvious distress except on moving or being moved, when pain was apparent. There was exophthalmos, and the skin was dry, with slight hirsutism of the face and chest. The nose and throat were normal. There were numerous irregular, tender swellings over the scalp, mandible, seventh cervical spine, left clavicle, left lower-chest wall in the midaxillary line, both tibias at their upper ends and the middle of the left femur. Moderate tenderness on pressure was present over both crests of the ilium, more marked on the left. The heart was slightly enlarged, with a blowing systolic murmur best heard in the pulmonic area and along the left sternal border; the blood pressure was 110 systolic, 70 diastolic. The lungs were normal. There was moderate tenderness, without spasm, in both lower quadrants of the abdomen. Pelvic examination was negative.

Examination of the urine showed a specific gravity between 1.008 and 1.028, with ++ to ++++ tests for albumin. The sediment was often "loaded" with white blood cells and occasionally with red blood cells. A phenolsulfonephthalein test showed 5 per cent excretion in fifteen minutes and a total of 20 per cent in half an hour. Repeated, there was a 15 per cent excretion in thirty minutes and a total of 25 per cent in an hour. Numerous Sulkowitch tests for urinary calcium varied from + to +++.

The blood showed a red-cell count of 2,300,000 with a hemoglobin of 55 per cent, and a white-cell count between 6000 and 14,000. A stained film was normal, and the reticulocyte counts varied between 2.0 and 5.2 per cent. The sedimentation rate was 8 mm. in one hour, the prothrombin time 40 seconds (normal, 20 seconds), and the hemato-

crit reading 37.5 per cent. The nonprotein nitrogen of the blood serum was 29 mg, the cholesterol 59 to 100 mg., the calcium 145 mg, the phosphorus 21 mg, the phosphatase 11.8 Bodansky units, and the protein 6.2 gm per 100 cc. The chlorides were 110.9 milliequiv, and the carbon dioxide combining power 22.8 milliequiv per liter. The serum van den Bergh was 2.1 mg. per 100 cc, biphasic; a bromsulfalein test showed 50 per cent retention; and a Congo red test showed 90 per cent retention of the dye in the serum. A gastric analysis showed free acid; the stools were normal. The basal metabolic rate was +32, +19 and +24 per cent on three occasions.

X-ray films of the bones showed a large defect in the skull in the right frontoparietal region, and a smaller defect in the upper frontal region. The entire calvarium was grossly thickened, and the margins of the inner and outer tables were obliterated. The bones showed a generalized decalcification, with large cystlike areas of rarefaction in the iliums, femurs, bones of the pelvis, ribs, scapulas and humeri. There was extensive rarefaction of the upper shaft of the left humerus, with destruction of the cortex on the lateral aspect. The bones of both forearms and hands showed changes similar to those in the other bones. An area of increased density was present in the distal extremity of the left radius, and a similar area in the distal extremity of the humerus. The lesions in the ribs and the upper extremity of the left tibia and both iliums showed marked thinning of the cortex, with expansion of the bones. The left acetabulum was thin, with intrapelvic protrusion of the left side of the pelvis in the region of the acetabulum. The vertebrae showed increased density in contrast to the other bones, and the trabeculations were irregular. Pathologic fractures were present in the second and the third lumbar vertebra, and the body of the fourth lumbar vertebra showed marked decalcification. The bones of the right foot showed decalcification, and there was a cystlike area in the distal extremity of the tibia.

With an intravenous pyelogram, the kidneys were obscured by gas in the intestine. There were two areas of calcification in the mid abdomen, and one overlying the sacrum, all of which had the appearance of calcified lymph nodes. There was also a 2-cm oval area of calcification overlying the transverse process of the fifth lumbar vertebra on the left, approximately in the course of the ureter. This shadow was somewhat denser and more smoothly rounded than the other shadows. Intravenous dye appeared on the right, and the kidney pelves and calyces appeared normal. There

was no evidence of excretion of the dye on the left.

Fluoroscopy and barium in the esophagus failed to outline a pathologic mass in the upper mediastinum. Laminograms of the anterior mediastinum failed to show evidence of disease.

X-ray films of the bones taken at another hospital three years previously showed that the osteoblastic areas present at that time in the lower radius and right tibia were typical benign giant-cell areas.

An electroencephalogram was normal.

On admission, the patient was very ill, and on the fourth hospital day a 500 cc blood transfusion was given. At the end of a week, a biopsy was taken from the left ilium.

#### DIFFERENTIAL DIAGNOSIS

DR WYMAN RICHARDSON: "Three years before entry, and without untoward symptoms, the patient gave birth to a normal child by forceps delivery; during her confinement she suffered from severe pyorrhea." Just what that means, I am not sure. It may mean that pre-existing bone disease was aggravated by pregnancy and resulted in pyorrhea. "... another parathyroid exploration was unsuccessful." I do not know where they looked for it. I am interested in knowing whether the sternum was split.

DR TRACY B. MALLORY: It was—on at least one occasion.

DR RICHARDSON: There is no record of the temperature. I assume that it was normal.

DR OLIVER COPE: The patient did have a little fever, but seldom more than a degree above normal.

DR RICHARDSON: "X-ray films of the bones taken at another hospital three years previously showed that the osteoblastic areas present at that time in the lower radius and right tibia were typical benign giant-cell areas." Do you know what that means, Dr Lingley, or should I ask you?

DR JAMES R. LINGLEY: The cystic areas spontaneously filled in with new bone, which is unusual. I suspect that the patient had a fracture.

DR RICHARDSON: I do not consider myself an expert on bone diseases. However, I shall try to see what I can do. There are four things that one should try to explain: bone disease, liver disease, as shown by the bromsulfalein retention; bone marrow disturbance, as evidenced by the severe degree of anemia; and kidney disease.

I shall start with bone disease. Perhaps we might look at some of these lesions, if Dr Lingley will be so good as to show the films. I particularly want him to tell me if the lamina dura is absent.

DR. LINGLEY: This is a generalized condition of bone characterized by multiple large cystlike areas of destruction. The process is most extensive in the pelvis, where one can see tremendous cystic areas in both iliums and intrapelvic protrusion of the acetabulum. In the spine, the decalcification involves the central portions of the vertebrae more than the margins, so that the margins appear denser in contrast. Some of the vertebrae show pathologic fractures. In the lower extremity of the radius, there is one area of increased density. The process is otherwise one of decalcification. The new-bone formation in this one area may have been due to a healed fracture. The process in the skull is characterized by generalized thickening of the calvarium and a large area of destruction in the frontoparietal region.

DR. RICHARDSON: The patient had teeth, and the lamina dura was absent. Is that not true?

DR. LINGLEY: Yes; and I did not mention an area of calcification in the region of the left ureter. That has the appearance of a calculus. The kidney is nonfunctioning on the left side.

DR. RICHARDSON: In regard to the bone disease, it is evident that this patient had overactive parathyroid tissue. The serum calcium was high, the phosphorus low. The phosphatase of 11.8 units seems to me to be a low figure in view of the degree of bone involvement, and that bothers me a little. However, I cannot see how you can get this picture with any widespread tumor process, and I therefore think it is a parathyroid effect. The fact that she was thoroughly explored and no adenoma found does not, I believe, rule out the possibility that one of these tumors was hidden and not found.

The next question to be considered is whether this might have been some type of secondary hyperplasia of the parathyroid glands, but I cannot see any good reason for such secondary hyperplasia and I have to rule it out. Therefore, I should say that this patient had primary hyperparathyroidism, probably due to a parathyroid adenoma, and that one should continue looking for it.

There are other things that are more difficult for me to explain. She had a marked anemia, apparently of a macrocytic type, with some evidence of reticulocyte increase. If one were to look at the blood smear, one would probably find evidence of bone-marrow activity. I do not recall an anemia of that type associated with parathyroid disease, and it seems to suggest that there is more evidence of encroachment on the bone

marrow than would be explained by cystic changes such as she showed. I do not see why disease of the bone of this type should interfere with marrow function to this extent, and I am bothered by that. I shall go back to it in a minute.

In regard to the liver, the serum van den Bergh was slightly above normal, and there was 50 per cent retention of bromsulfalein, so that there is evidence of some disturbance of hepatic function. We know this patient had a renal stone, presumably because she had been excreting so much calcium. One kidney is said not to have excreted any dye. On the other hand, excretion of phenolsulfonephthalein dye was fairly good, considering the renal function as a whole—20 per cent in half an hour, and 25 per cent in another test; function was definitely impaired, but not markedly so. The urine could be concentrated up to 1.028. At the same time, the patient had marked albuminuria, and the blood pressure was 110 systolic, 70 diastolic. There was no hypertension. She was entitled, of course, to some kidney infection along with the stone. It seems to me that the renal picture, with that degree of albuminuria, with normal blood pressure and with normal nonprotein nitrogen, is the picture one sees with nephrosis. If one considers that as a possibility, one begins to wonder whether there was some other condition that involved the kidney, the liver and the bone marrow. A Congo red test gave 90 per cent retention of the dye. If one considers it specific for amyloid disease, one would have to say that for some reason this patient had amyloid disease. Usually, of course, amyloid disease is associated with infection, and I cannot make out that this patient could have had a long-standing infection. I do not see any reason to consider amyloid disease.

DR. COPE: I should have spoken up sooner. Ninety per cent of the dye was still found within the serum. We considered it normal.

DR. RICHARDSON: The Congo red test, then, is against amyloid disease, and it is foolish to talk about it anyway. As a matter of fact, I do not consider the Congo red test to be worth anything. It may possibly be valuable when 90 per cent, or so, of the dye is taken up. However, since I can think of no other explanation of hepatic involvement, I raise a question of amyloid disease.

I shall leave my discussion there and say that this patient had primary hyperparathyroidism probably due to adenoma, with secondary renal calculus and bone changes.

DR. J. H. MEANS: I should like to know more about the thyroid situation. There is just enough given here to be tantalizing, but hardly illuminat-

ing. It is a mystery why they took out the thyroid gland, why the patient had exophthalmos, and why the metabolic rate went up rather than down after thyroidectomy.

DR. RICHARDSON: I meant to mention the exophthalmos. I wonder if she had always been a little exophthalmic; and if not, could it not have been due to some lesion in the orbit?

DR. FULLER ALBRIGHT: She had an unusually thick skull.

DR. LINGLEY: There is thickening of the bones all around the orbits. I do not see any reason why that might not be the cause of the exophthalmos.

DR. RICHARDSON: As for the basal metabolic rate, I wonder whether it was basal. She had a severe anemia and a fever.

DR. ALBRIGHT: I believe they took out the thyroid gland in looking for the parathyroid tumor. They thought it might be in the thyroid gland.

A PHYSICIAN: How do you explain the continuous severe headaches?

DR. RICHARDSON: There was enough bone disease to account for that. Is it true that people with high blood-calcium levels have headaches?

DR. ALBRIGHT: I do not believe so.

A PHYSICIAN: Was a lumbar puncture ever done?

DR. COPE: She could not be rolled over. It was very difficult even to take x-ray pictures. She was very ill, and the plates were taken one or two at a time.

DR. WILLIAM B. BREED: Could the large skull lesion account for the headaches?

DR. ALBRIGHT: Yes; it most certainly could. There is a huge blood supply to this type of lesion.

We came to the same conclusion as Dr. Richardson, with exactly the same misgivings. There were four reasons why we were puzzled. In the first place, the patient had been operated on at two excellent clinics and no tumor had been found. That is only a fairly good reason. Secondly, the skeletal x-ray films showed localized areas of normal bone density. One can have a patient with hyperparathyroidism and no bone disease, but if there is bone disease it should be generalized. Dr. Cope finally explained these areas by going back to previous x-ray films and finding that there had been cysts in these same areas. Thirdly, we were also disturbed about the phosphatase. It was high, but not so high as we should have expected for the degree of bone disease. But the thing that disturbed us most of all was the anemia. When one meets bone disease with anemia, one worries, of course, about some bone-marrow tumor. However, a bright thought was finally brought forth to

explain the anemia. After all, this patient was a mass of giant-cell tumors. These are very vascular lesions and have many hemorrhages into them. This gives them their characteristic brown color, which is due to changed hemoglobin. We, therefore, finally concluded that her anemia was due to blood loss into her bones.

DR. RICHARDSON: The anemia as described could not be due to chronic blood loss.

DR. ALBRIGHT: I wonder if the figure for the hematocrit is correct.

DR. MALLORY: There are two figures recorded here—a hematocrit of 20 per cent, corresponding to a red-cell count of 2,300,000, and one of 37.5 per cent, going with a red-cell count of 3,400,000. The second pair of figures followed several transfusions.

DR. RICHARDSON: The hematocrit was approximately normal then, whereas an anemia due to blood loss should be definitely microcytic and hypochromic. Is there a description of the blood smear?

DR. ALBRIGHT: Dr. Bernard M. Jacobson reported normocytic, normochromic red cells and no immature red or white cells except for the reticulocytes, which were always high varying from 2 to 5 per cent. The serum van den Bergh was a little high, 2.0 mg., and the urobilinogen was increased, a finding suggesting increased blood destruction.

DR. RICHARDSON: The blood picture as reported by Dr. Jacobson is nonspecific, and without examining the smear myself I hesitate to make further comment.

DR. COPE: Dr. Albright comforted me a great deal by being worried, because we certainly were worried. It is fair to emphasize that, in addition to the increased bone density in the three areas, the patient had four huge giant-cell tumors of a size that we have not encountered in any other patient with hyperparathyroidism. It occurred to us that perhaps she had malignant bone disease originating in the giant-cell tumors, and I hope that Dr. Mallory will discuss this, because roughly 7 per cent of the benign giant-cell tumors of adolescence become malignant. We have not, curiously enough, encountered the development of bone malignancy in any of the areas of microscopically similar giant-cell tumors in hyperparathyroidism. Patients with hyperparathyroidism may have hundreds of these tumors.

In the x-ray films, the large tumor areas appear to be cystic. When we cut down on the one in the ilium, it was a huge solid tumor like a very stiff sponge, very vascular, with a thin cortex of bone. We were interested to know



tune and eating very little. The question is whether a quart of milk a day would be sufficient to produce the necessary extrinsic factor for blood formation. It might be a macrocytic anemia due to the lack of the food factor described by Castle \*

DR ALBRIGHT. But she had reticulocyte response

DR RICHARDSON: That is the feature of myelophthisic anemia. Such patients have reticulocytes, nucleated red cells, polychromatophilia and so forth

DR ALBRIGHT. I shall have to read my book again

## CASE 27312

### PRESENTATION OF CASE

A fifty-three-year-old woman entered the hospital complaining of "dizzy spells"

The patient felt well until the birth of her first child, sixteen years before admission. Ever since that time, she had suffered from attacks of weakness and palpitation and from a sensation of fainting. The attacks lasted ten to fifteen minutes, came on in any position and at any time, and were relieved by lying down. One year after the onset, the patient was admitted to a hospital for three months, where a diagnosis of cancer was made and x-ray treatments were given to her left chest. This resulted in complete relief for the next five years, at the end of which time the attacks reappeared. Sixteen x-ray treatments were directed at the same region in her chest, and again there was relief and she was "able to breathe better." The patient then felt well until eight months before admission, when the "spells" recurred. She consulted her physician, who said that her "left chest had filled up again," and subsequently sixteen x-ray treatments were given. This time, there was no relief, and operation was advised. At no time had there been pain, cough, hemoptysis, dyspnea, orthopnea, edema, nausea, vomiting, tarry stools or loss of weight.

The family history and past illnesses were irrelevant

On examination, the patient was well developed and well nourished and in no distress. The left border of the heart could not be made out, but the organ was displaced to the right. There were no murmurs, and the rhythm was irregular, without pulse deficit, the blood pressure was 140 systolic, 84 diastolic. Examination of the lungs

showed dullness to percussion, absent tactile and vocal fremitus, and absent breath sounds over the entire left chest anteriorly from the level of the first rib down and posteriorly from the level of the third dorsal vertebra.

Examination of the abdomen and nervous system was negative.

The temperature was normal, the pulse 94, and the respirations 23

The urine gave a + test for albumin. The blood showed a red cell count of 4,340,000 with a hemoglobin of 13.0 gm (photoelectric cell technic), and a white cell count of 16,600. A blood Hinton reaction was negative.

An x-ray film of the chest showed an unusually large mass occupying the lower three fourths of the left side of the chest and displacing the heart shadow to the right. The upper margin of the mass was sharply defined and smoothly rounded, without lobulations, and the greater portion of the tumor lay anteriorly. It was homogeneous in density, and no areas of calcification were seen within it. The right lung field was clear.

A barium swallow showed the esophagus to be displaced to the right along with the heart shadow. The mass itself, however, did not appear to extend as far medially as the esophagus.

On the seventh hospital day, an operation was performed.

### DIFFERENTIAL DIAGNOSIS

DR RICHARD H. SWEET: There were no symptoms referable to her chest, hence, we are dealing with a mediastinal tumor, and I presume that much of the differential diagnosis depends on the examination of the x-ray films. May we see them, Dr Hampton?

DR AUBREY O. HAMPTON: All these films were taken within three days, so that we had no time control. The mass does lie anteriorly. Although you probably cannot see it from your seats, this is the posterior margin, very sharp and smooth. Variation in position of the patient did not seem to change the shape of the mass. It remains at about the same level in all the films. It does not seem to move with respiration. The esophagus is displaced, and the visible portions of the lungs are perfectly normal. There is no evidence of disease in the ribs or spine. We cannot see the anterior ends of the ribs very well, and a mass lying anteriorly might involve them without showing. I do not believe that is the case here. The ribs are thin, as they often are in this area, but they are not separated.

DR SWEET: The history is puzzling because of its long duration and because of the statements

\*Castle W. B., Townsend W. C. and Heath C. W. Observations on the etiology relationship of achylia gastrica to pernicious anemia. III. The nature of the reaction between normal human gastric juice and beef muscle leading to clinical improvement and increased blood formation similar to the effect of liver feeding. *Am. J. M. Sc.* 180:305-335, 1930.

made about the benefits obtained from x-ray treatment. I cannot believe that the patient had anything that should have been treated by x-ray sixteen years ago. If she had cancer at that time, as the record suggests, she would not be alive and well sixteen years later, either with or without x-ray treatment. So that I doubt very much if she had cancer sixteen years before she came in. For the same reason, I also doubt very much if she had lymphoma at that time, although some tumors of the lymphoma group do survive for relatively long periods. Furthermore, I do not understand why x-ray treatments given sixteen years ago afforded relief from her dizzy spells, palpitation and sensations of fainting. Nor is it easy to explain the ten-year period of freedom from symptoms before there was a recurrence, once again with relief after x-ray treatment. I am forced to conclude that the dizziness and related symptoms bore no relation to the mediastinal tumor, and that x-ray treatment of the chest to relieve them was irrational.

It seems to me that in the differential diagnosis we must first exclude a chest-wall tumor. The x-ray films do that satisfactorily. The physical signs are those of tumor. The films suggest that it is a solid tumor, and one can fairly well exclude tumor of the lung, because of the lack of symptoms and because of the x-ray findings. We therefore have to assume, if we exclude these two sources, that this tumor arose primarily from the mediastinum, although it has pushed into the left chest rather far. The heart and other mediastinal structures have been pushed to the right. The statement is made, and it seems apparent from the x-ray films, that the tumor was in the anterior part of the chest, although it has grown posteriorly to some extent. I assume it did not arise in the posterior part. Solid or cystic tumors arising in this region are relatively few, as you know. We have seen tumors—not of this size, in my experience—arising from the thymus. Last summer, we had a dermoid cyst in the mediastinum arising from thymus remnants, but that was no bigger than a baseball. This is too big to be a thyroid tumor. I suppose lymphoma might be mentioned, but it does not look to me like lymphoma, in spite of the long history and the relief after x-ray therapy. It could be a dermoid cyst. It shows no calcification, but that is not necessary by any means. If it had arisen from the posterior mediastinum, we should have an excuse for mentioning neurofibroma, since tumors of that group commonly occur in the posterior mediastinum. At any rate, although I cannot make a definite diagnosis of what the tumor is,

I should say it was a solid or cystic tumor, and that the patient ought to be operated on.

DR. TRACY B. MALLORY: Dr. Bland, you saw this patient in relation to the attacks of dizziness and fainting.

DR. EDWARD F. BLAND: For fifteen years, she had had paroxysmal attacks of rapid heart action, which I assume were responsible. On examination, I did not find anything wrong with her heart. Later, she had an attack of tachycardia that lasted fifteen minutes, but when I saw her, her heart action was again normal, the blood pressure was all right, and her condition was good. I ordered 3 gr. quinidine, three times a day, as a prophylactic measure.

DR. RALPH ADAMS: As Dr. Churchill's associate, I saw this patient and believed preoperatively that she had a dermoid cyst. I also thought of teratoma.

DR. EDWARD D. CHURCHILL: We had the advantage of seeing an x-ray film taken five years previously, which was apparently identical with the ones you see here. Several needle aspirations had been attempted, but her physicians never obtained anything but blood, so that we did not try thoracentesis. We were faced with a rather difficult situation in regard to indications for operation because this woman was getting along quite well except for her attacks of dizziness. It was known that the mass had been present for at least five years, and she was fifty-three years of age. She had been prepared for operation in another city, but a heart attack led to cancellation of the program. Our line of reasoning was a good deal the same as that in a case of dermoid cyst presented here a few weeks ago. That is, this patient was reaching an age at which she might be expected to have more frequent symptoms related to her heart, and for the rest of her life her medical advisers would face the dilemma whether to take the tumor out or to let her carry on and accept any cardiac embarrassment that the tumor might be causing. Also, it was impossible to disassociate symptoms that might arise from intrinsic heart impairment and heart action disturbed by the presence of the huge tumor. However, we assured her physician that we reserved the privilege of making a dignified retreat if we thought the removal of the tumor would in itself be too hazardous. In other words, we did not want to assume a foolish risk with an eye on the trophy because of the relatively comfortable life that this woman was able to lead. When we did open the chest, it was found that the tumor was readily resectable. She made an uneventful recovery. I do not believe we made a definite preoperative

diagnosis—any more definite than that made by Dr Sweet

DR ADAMS 'Excision of mediastinal tumor is written on the operative sheet. As we discussed it preoperatively, I believe we learned toward termination

DR MALLORY Can you describe the location of the mass at operation?

DR CHURCHILL It seemed to be from the anterior mediastinum. It filled the whole hemithorax.

DR MALLORY Could it have arisen from the sympathetic chain?

DR CHURCHILL No, it was too far anterior. The phrenic nerve was displaced backward by the tumor.

#### CLINICAL DIAGNOSIS

Mediastinal tumor

#### DR SWEET'S DIAGNOSIS

Benign tumor of the anterior mediastinum (possibly dermoid cyst)

#### ANATOMICAL DIAGNOSIS

Perineural fibroma

#### PATHOLOGICAL DISCUSSION

DR MALLORY The tumor, as is of course obvious from the x-ray films, was an extremely large one. Its whole central portion was necrotic—a mass of dead tumor tissue and hemorrhage, around which lay a rim of viable tumor of varying thickness. There were some spots that looked yellow in gross, and one area almost suggested the membranous lining of a cyst so that the question arose whether it might be a dermoid. On microscopic examination, however, it is quite obvious that it is a fibromatous tumor and equally obvious that it is of neurogenous origin, in fact, one might, I believe, classify it as schwannoma, although

such tumors do not usually grow to this size or show necrosis in the center. The outlook I think is good. It is unlikely that there will be a recurrence.

DR CHURCHILL It is not a malignant tumor?

DR MALLORY I should say not. Our original impression, I confess, was fibrosarcoma.

DR CHURCHILL Have you taken several sections in varying parts to be sure that there was only one germ layer involved?

DR MALLORY We have gone back to the gross specimen and picked more suspicious areas from that point of view, and found no other form of tissue. The tumor is obviously of nerve sheath origin.

DR HELEN S. PITTMAN Then it could not have responded to x-ray therapy?

DR MALLORY It seems improbable.

A PHYSICIAN Where did it arise?

DR MALLORY There are sympathetic nerves everywhere, and it did not have to arise from a grossly namable one.

DR BLAND Have the attacks of rapid heart action been less frequent since the operation?

DR CHURCHILL I have not had a follow up report yet.

DR BLAND In one attack during her hospital stay, we were able to get an electrocardiogram, which showed that her rapid heart action was due to auricular flutter. Several of the recent cases of flutter we have recorded have been in patients who have had something seriously wrong in their chests and have been operated on.

DR CHURCHILL It comes as a postoperative complication not infrequently.

DR ADAMS Of the four cases of flutter that Dr Bland and I have been thinking of, two occurred in association with anterior mediastinal tumors, one in a thoracoplasty in which the apical adhesions had required considerable dissection anteriorly, and the fourth in a case of lobectomy for bronchiectasis.



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## WARTIME TRANSFUSION THERAPY

EVEN war has its mitigations. In the present carnage, it is probable that much will be learned regarding surgical shock and its treatment by the injection of blood or one of its components.

Ten or fifteen years ago, certain Russian investigators drew blood from healthy cadavers; this was citrated, stored and given to patients, with good results. The possible value of this maneuver on the battlefield was obvious. Stored citrated blood obtained from healthy living persons was also used with success; the war in Spain proved that the method could be adapted to use on a large scale. During this period, the British medical journals began to publish numerous articles dealing with blood banks, and long before the present

war began, the British medical profession had prepared for trouble by equipping each section of London with a decentralized blood bank and a supply of volunteer donors. In this country, the first successful blood bank was organized a few years ago at the Cook County Hospital in Chicago, and since then, a number have been in successful operation.

For a hospital of at least two hundred beds in which there is a fairly large volume of surgery and obstetrics, the blood bank is very useful, particularly to the overworked intern. The bank, nevertheless, has its limitations. Blood gradually deteriorates even when stored at 2 to 4°C.: the immune bodies and prothrombin diminish considerably, the leukocytes and platelets disappear quickly, and the red cells become spheroidal and thus readily broken up in the circulation. For these reasons, fresh blood is distinctly preferable in the treatment of blood dyscrasias, chronic anemia and those acute infections in which the antibody or prothrombin content of the injected blood may be of some importance. Furthermore, transfusion reactions appear to be commoner with bank blood, and there is still the necessity for typing and cross-matching.

During the last year or two, the value of serum or plasma transfusions has been clearly demonstrated. For surgical shock, in which the symptoms are chiefly due to the loss of plasma from the circulating blood, it is of the utmost importance to inject intravenously a substance that remains in the circulation. The red blood cells are not needed, unless there has been serious hemorrhage, and blood serum or plasma is the ideal material. Furthermore, the use of pooled serum or plasma has several advantages. In the first place, it can be transported easily and stored for long periods—practically indefinitely in dried form. Secondly, since pooled samples lose their blood-group characteristics, it can be given quickly and indiscriminately, without wasting time for typing and cross-matching. Thirdly, it can be injected, if desired, in two or three times its normal concentration. Appreciating these facts, the

British Red Cross appealed last summer to the American Red Cross for a supply of plasma, and up to February of this year, when plans had been perfected for obtaining the supply in England, the American Red Cross, in co-operation with the Blood Transfusion Betterment Association, collected and shipped approximately 15,000 pints of liquid plasma

With the shipments to England ended, the American Red Cross, at the request of the Surgeons General of the United States Army and Navy, has now undertaken to provide a national reservoir of blood plasma for emergency use. It is being prepared in two forms: ordinary fluid plasma and dry, powdered (lyophilized) plasma, which is made ready for immediate use by the addition of sterile distilled water. Thus, thanks to the American Red Cross and affiliated agencies, the Army and Navy will have available quantities of plasma, ready for instant use

For the treatment of anemia, leukopenia and thrombopenia and of infectious processes, fresh blood obtained directly from healthy donors is still preferable. For emergency use in surgical shock, even when accompanied by a moderate amount of hemorrhage, plasma is probably as useful as whole blood. Thus the importance of a bank for storage of whole blood will probably diminish as dried plasma becomes commercially available

Blood in "tin cans"! Thus does science advance even as moral values reach low ebbs. The American Red Cross is to be congratulated for its sponsorship of still another humane project, which will certainly find its ultimate value in days of peace

## HANS BERGER

HANS BERGER,\* one of the foremost neuropsychiatrists of our time, discoverer of the electrical waves of the human brain, died on July 7, in Jen<sup>a</sup>, at the age of sixty eight. His important contribution to medicine, when first reported in 1929,

was considered by many as ludicrous. In the last ten years, however, it has been shown not only that his discovery was sound, but that, because the rhythmic, electrical discharge is altered in various normal and abnormal mental conditions, particularly in epilepsy, a new and highly significant technic, electroencephalography, had been made available for neurologic and psychiatric investigation.

To some of his contemporaries, this great achievement seemed like a stroke of luck, but viewed in terms of his earlier work and his life method it was the end result of a long and persistent search. From his days as a *Privatdozent* onward, he was a determined experimentalist. He proceeded on the assumption that the brain is a physicochemical machine, of which the chief product is behavior; and he was continually looking for what he called the physical concomitants of mental activity. His first studies were on the cerebral pulse, and he used its wave form and the interval between it and the apex beat to indicate the state of the cerebral vascular bed. Two of his early books, *The Intracranial Circulation* (1901) and *Organic Manifestations of Mental States* (1904-1907), contain reports of this work. His experiments on cerebral circulation were by no means impressive, but this was largely because no major changes in cerebral blood flow occur in association with the conditions he studied, namely, mental work, fright, sleep and states initiated by various types of sensory stimuli. These facts could not have been proved from deductive reasoning

Berger next turned his attention to the study of the temperature of the brain, and again he failed to find important correlations. Despite these negative results, three books, entitled *Studies on the Temperature of the Brain* (1910), *Trauma and the Psychoses* (1915) and *Localization in the Cerebrum* (1927), revealed in his work a persistently physiologic point of view

In 1924, at the age of fifty one, when many determined experimenters weaken and lapse into speculation, Berger started his epoch making work

\*An exhibit of material depicting Berger's discovery is now on display in the rotunda of the Boston Medical Library through the kindness of Dr. Frederic A. G. Lila

on the electrical activity of the brain. His search for electrical accompaniments of mental activity was, as a matter of fact, a return to a youthful line of investigation that he had started in 1902.

The significance of Berger's discovery was vaguely grasped by Adrian and Matthews, in England, in 1933, and the name, "Berger's rhythm," was given to the electrical discharge of the brain by the same authors in 1934. They, erroneously, thought that the waves originated in the occipital lobe and were identified with vision. By 1936, electroencephalography was firmly established in this country as a clinical and experimental technique, and much of the subsequent knowledge of the Berger phenomenon has originated in the United States.

Berger's discovery has become a cornerstone in the slowly growing structure of neurologic and psychiatric knowledge and affords a new basis for the dynamic approach to the study of brain function.

## MEDICAL EPONYM

### JACKSON'S MEMBRANE

Jabez N. Jackson (1868-1935), of Kansas City, Missouri, read a paper before the Western Surgical Society at Minneapolis, Minnesota, in December, 1908, entitled "Membranous Pericolitis." This was printed with revisions and additions in *Surgery, Gynecology and Obstetrics* (9: 278-287, 1909).

Wherever . . . we find any late manifestations of peritoneal disturbance about the colon we have been content to label it "adhesions," presume an antecedent acute appendicitis, and pass on. Some very striking . . . observations . . . have persuaded [the writer] that there is a most interesting pathological condition occurring about the right colon which can not thus readily be set aside. . . . The following description . . . is . . . from the report of Dr. Frank Hall, pathologist. . . . "From a point just at the hepatic flexure to three inches above the caput there spreads from the parietal margin over the external lateral margin to the internal longitudinal muscle band a thin vascular veil."

Synchronously with our recognition of the distinct pathology and clinical identity of this condition, we had been impressed with the view that this pericolonial membrane by its mechanical interference with colonic peristalsis was possibly, if not probably, responsible for the chain of symptoms which were manifest when it was found present.

R. W. B.

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

#### ATTEMPTED FORCEPS DELIVERY AND CESAREAN SECTION, FOLLOWED BY DEATH

A forty-year-old para IV entered the hospital at term, after being in labor for twenty-four hours at home. She was under ether when admitted.

The prenatal care during this pregnancy had been inadequate. The past history was irrelevant. The three previous pregnancies had terminated in normal deliveries, none of the babies weighing more than 6 pounds.

Prior to admission, the patient's family physician had unsuccessfully attempted forceps delivery, and the patient arrived at the hospital with the cord prolapsed. According to the admission note, the cervix was dilated to admit two fingers, the head was high, and a nonpulsating cord presented. The pulse rate was not recorded. A classic cesarean section was immediately performed, and an 8-pound, 5-ounce, stillborn baby was delivered. A drain was placed in the pelvis. During the first two weeks of convalescence, there was some febrile reaction, but no evidence of a generalized peritonitis. On the fourteenth day, the wound broke down, and evisceration of the bowels occurred. The bowels were replaced, the wound was resutured, and the patient was transfused. She died nineteen days after operation, the death certificate stating that she died of bronchopneumonia.

*Comment.* From beginning to end, this case represents poor obstetrics. The apparent size of the child, particularly in view of the fact that the three other babies were small, and the height of the head should have stimulated inquiry and possibly x-ray study. This patient undoubtedly had some form of contracted pelvis. When she entered the hospital, the cervix was said to have been only slightly dilated. This probably meant that the cervix had shut down after the attempt at delivery had failed, because it is not imaginable that anyone would attempt forceps delivery with such a dilatation of the cervix.

There were two ways of treating this patient after she arrived in the hospital with the cord prolapsed, the baby dead and the uterus probably infected. One would have been an extraperitoneal section of the Waters type, accompanied by transfusion. If this had seemed to be contraindicated, cesarean section with hysterectomy would have been the operation of choice. This is a death resulting from intraperitoneal cesarean section, which was contraindicated from the outset.

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, Secretary, 330 Dartmouth Street, Boston.

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## THERAPEUTIC CONSIDERATIONS OF THROMBOPHLEBITIS AND PHLEBOTHROMBOSIS\*

ALTON OCISNER, M.D.,† AND MICHAEL DEBAKEY, M.D.‡

NEW ORLEANS, LOUISIANA

AS emphasized in previous publications<sup>1-4</sup> from etiologic, prognostic and therapeutic stand points, it is important in intravenous thrombosis to distinguish between two major types of intravascular clotting, that is, thrombophlebitis and phlebothrombosis. The clotting in thrombophlebitis is the result of injury to the vascular endothelium from mechanical trauma, bacterial invasion or chemical injury, whereas in phlebothrombosis the intravascular thrombus formation is due to venous stasis and to alterations in the cellular and fluid constituents of the blood that increase the clotting tendency. The prognostic significance of this differentiation lies in the fact that in thrombophlebitis the clot is usually firmly adherent to the vein wall and is therefore less likely to be come detached and result in embolism. On the other hand, in phlebothrombosis the coagulum is loosely attached to the vessel and is therefore likely to cause embolism. The therapeutic significance of this differentiation lies in the recognition of the respective processes and the institution of appropriate measures to prevent the occurrence of complications and to enhance restitution.

In this presentation, no attempt is made to discuss etiology and pathogenesis because these have been reviewed in previous publications<sup>1-4</sup> and will be presented more extensively in subsequent reports.

### PROPHYLACTIC MEASURES

#### *Preoperative Procedures*

*Re establishment of normal cardiovascular function.* The possibility of intravenous clotting must be considered in any patient who has tissue injury as a result of operative, accidental or puerperal

trauma, and invasion by infection or neoplastic disease. Whereas preventive measures cannot be considered in many of these conditions, much can be accomplished prophylactically in the surgical and puerperal cases. Because cardiovascular disease, with its resultant circulatory retardation, may be a precipitating factor, it is essential to re-establish the *normal cardiovascular function* as much as possible before any operative procedure. Welch,<sup>5</sup> in 1900, reported 4 cases of thrombosis or thrombophlebitis of the upper extremity and collected 23 from the literature. At that time, he regarded this as a rare complication of heart disease. Belt<sup>6</sup> obtained a history of cardiac impairment in 49 of 56 cases of pulmonary embolism. He is of the opinion that circulatory embarrassment is of primary importance in the etiology of venous thrombosis and pulmonary embolism. Cardiovascular disease was the predominant illness in half the nonsurgical cases of pulmonary embolism studied by Henderson.<sup>7</sup> Ophuls and Dobson<sup>8</sup> found cardiovascular disease in 52 per cent of their cases of thrombosis and embolism. Putnoky and Farkas<sup>9</sup> noted that approximately 90 per cent of 91 cases of pulmonary embolism had cardiovascular disease, and a large number of these showed fatty degeneration of the myocardium. Bauer<sup>10</sup> found that the patients in 95 of 100 cases of postoperative thrombosis and embolism had abnormal hearts. He is of the opinion that impairment of cardiac function is an important factor in the etiology of venous thrombosis. Oberndorfer<sup>11</sup> observed that of 97 fatal medical cases of pulmonary embolism, 64 patients had cardiovascular disease at the time of the terminal seizure. Rosenthal<sup>12</sup> reported 94 cases of thrombosis in 149 autopsies performed on patients with cardiac decompensation. Aukhausen<sup>13</sup> reported 270 cases of venous thrombosis in 1472 autopsies on patients with heart disease. Storz<sup>14</sup> emphasizes that the incidence of thrombosis is dependent more on the condition of the heart and

\*The Shattuck Lecture delivered at the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1941.

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the circulatory system than it is on the disease process or the operation. Kuhn<sup>15</sup> found that in autopsy material, between the years 1919 and 1927, — during which there was a definite increase in vascular diseases, particularly arteriosclerosis, — there was a marked increase in thrombosis. Burke<sup>16</sup> reported that of a total of 648 cases of intravascular clotting, 444 were associated with cardiac disease. His statistics further emphasize the importance of cardiovascular disease in the development of thrombosis, because in this series there were 218 patients who developed thromboses after escaping it following a previous operation. Of this number, 179 had cardiovascular disease as a primary or an important secondary condition. Barker and his co-workers<sup>17</sup> found that of 1665 patients with thrombosis and embolism, 219 (13.1 per cent) had cardiac disease.

Of great significance from the standpoint of cardiovascular disturbance is advancing age. It is well known that in older persons, because of the decrease in cardiovascular activity, thromboses are likelier to occur. According to Ewald,<sup>18</sup> intravenous clotting occurs in young people only when there is a circulatory disturbance. Koch<sup>19</sup> found that between the ages of fifteen and nineteen years the circulation time averaged eighteen seconds; between thirty and forty years it was twenty-one seconds, and at seventy years it was twenty-three seconds. In patients in whom there was a circulatory disturbance, the circulation time was frequently as much as sixty-one seconds, and after operation there was a definite interference with the circulation. Numerous other observers have emphasized the effect of cardiovascular disease in the production of intravenous clotting and the necessity for treatment of cardiovascular dysfunction.<sup>20-27</sup> Blumgart and Weiss,<sup>28</sup> from clinical investigations concerning circulation time, found that in general the degree of cardiac decompensation is of importance. These clinical observations emphasize the significance of cardiovascular diseases in the production of intravenous thrombosis and indicate the necessity of their detection and correction preoperatively. The value of prophylaxis in this connection is exemplified by von Jaschke's<sup>22</sup> results. Whereas in a series of 2053 operations the incidences of thrombosis and fatal embolism were 1.75 and 0.6 per cent respectively, in a comparable series of 1362 operations in which the patients were systematically digitalized preoperatively, the corresponding incidences of thrombosis and fatal embolism were 0.9 and 0.5 per cent. Koenig<sup>29</sup> found that, following the use of Sympathol in 2000 cases postoperatively, the incidence of thrombosis and embolism decreased from 6.2 to 0.95 per cent. Similarly, Frau-

endorfer<sup>30</sup> observed a decrease from 10.6 to 2.3 per cent and in the mortality from 2.3 to 0 per cent. Similar observations have been made by others.<sup>31, 32</sup>

Because of the definite vasoconstrictor effect of *smoking*, it is essential preoperatively, particularly before an operation in which there is likely to be considerable trauma, that smoking be stopped for a period of days or weeks. As has been emphasized in previous publications, smoking produces distinct vasospasm and thus favors vascular retardation, which in turn is an important factor in the production of intravenous clotting. Subsequently, when the treatment of intravascular clotting by vasodilatation is discussed, the role of vasospasm in the production of the condition will be emphasized.

In *varicosities* of the lower extremity with associated venous stasis,<sup>33</sup> the possibility of thromboses in the dilated veins must be considered. Barker et al.<sup>17</sup> found that of 1665 cases of thrombosis and embolism, 203 had simple varicosities of the lower extremity. The importance of varicosities as a factor in thrombophlebitis has been repeatedly emphasized.<sup>18, 21, 34-39</sup> For this reason, varicosities must be corrected preoperatively either by curative measures or by palliative compression with bandages, which should be worn during the early postoperative period. By so compressing and obliterating the dilated, superficial venous system, stagnation of blood in the superficial system is obviated and the rate of blood flow in the deep venous system is increased, both of which tend to decrease retardation. In this way the possibility of thromboses both in the superficial and deep veins is diminished.

The value of compression of the superficial veins in thrombophlebitis was first stressed by Fischer.<sup>40</sup> A great deal can be accomplished prophylactically by the use of compression bandages even in patients who have no varicosities, because by compressing the superficial veins the rate of flow in the deep veins is increased. Numerous observers have directed attention to the prophylactic value of compression,<sup>21, 26, 36, 37, 41-44</sup> particularly in the presence of *predisposition* to thrombophlebitis or phlebothrombosis. Leunt<sup>45</sup> states that for nine years he and his associates have been using compression bandages prophylactically in patients in whom they feared a thrombosis — these are patients who had varicosities, circulatory disturbances or other *predisposing factors*. In 280 cases, they applied five hundred elastic compression bandages. In 3 cases, the treatment was a failure in that a thrombosis occurred. In two of these, slight thrombosis occurred because the bandage was not applied tightly enough, and the third

patient died of a pulmonary embolism, but autopsy showed that the thrombus originated from a pelvic vein and not from a leg vein. Although Unna<sup>46</sup> and Lasker<sup>46</sup> have suggested the use of Unna's paste boot for its antiphlogistic action, most observers agree that the compression is the significant factor, and it is for this reason that an adhesive elastic bandage is usually preferred to a simple adhesive plaster.

As we<sup>1-4</sup> have previously stated, constitutional predisposition is a definite familial tendency.<sup>47-58</sup> These patients characteristically are fat, weak-muscled and pale skinned, and have a relatively low blood pressure, vagotonia and a psychic lability.

*Reduction in weight.* Numerous observers have directed attention to obesity as a predisposing factor in thrombosis.<sup>18, 41, 42, 59, 60</sup> Snell<sup>60</sup> found that of 150 obese patients who died postoperatively the cause of death was thromboembolism in 48 (31 per cent). Henderson,<sup>7</sup> in a statistical analysis of post-mortem thromboembolism cases, reported that the average weight of the patients was 13 pounds greater than normal. Barker and his co-workers<sup>17</sup> reported that obesity exerts a definite influence on the production of thrombosis and embolism. They observed that in patients who had an abdominal hysterectomy the incidence of postoperative venous thrombosis and pulmonary embolism was 4 per cent in patients who weighed less than 200 pounds and 8 per cent in those weighing more than 200 pounds. Of 3680 patients on whom intestinal operations were done, thromboembolism occurred in 3.2 per cent of those who weighed less than 200 pounds, and 7.1 per cent of those who weighed more than 200 pounds. Friedländer<sup>41, 42</sup> believes that in obese patients interference with the return flow of blood through the femoral veins is greater because the opening in the femoral canal is encroached upon by fat and because the fat bolster in the buttock is larger and thus results in greater elevation of the pelvis. This makes a higher angle in the femoral vein and thus further interferes with the flow of blood into the pelvis. According to Snell,<sup>60</sup> the increased incidence of thrombosis in obese persons is due to the greater difficulty in operating, to the greater likelihood of circulatory retardation and to the liberation of large quantities of lipid thromboplastic substances. Rösse<sup>61</sup> is of the opinion that in obese persons, because of the increased weight of the leg, the pressure of the calf muscles against the bed is sufficient to compress the veins, and thus predisposes to intravascular clotting. These observations emphasize the importance of obesity in the production of thromboembolism and indi-

cate the necessity of reduction in weight as a preoperative prophylactic measure.

*Elimination of foci of infection.* As emphasized in previous publications,<sup>1-4</sup> infections are contributory in the production of distant thromboses, because of the changes in the blood constituents resulting from destruction of tissue. For this reason, it is prophylactically desirable to remove all foci of infection whenever possible. Gougerot and Frumusan<sup>62</sup> reported a case of phlebitis studied bacteriologically and histologically in which an anaerobic streptococcus was found in an abscessed tooth, the intradermal reactions to this organism being strongly positive. Biopsy of the phlebotic vein showed the same organism. Of interest in this connection is the report of a case of migratory thrombophlebitis which was apparently due to a focus of infection in a tooth, since recovery followed its extraction.<sup>63</sup> The relative frequency of thrombophlebitis complicating typhoid fever has long been known. It has been recently emphasized by Conner,<sup>64</sup> who states that this incidence is as high as 10 per cent. It has also been recognized as a complication of Boutonneuse fever.<sup>65</sup> Barker and his co-workers<sup>17</sup> found that of 1665 cases of thromboembolism there were 379 (22.8 per cent) with severe infections. Other infections that are likely to be associated with thrombosis are influenza, acute rheumatic fever, syphilis and endocarditis. Bargen and Barker<sup>66</sup> have stressed the importance of thrombosis as a complication of chronic ulcerative colitis; they observed 18 cases with severe thromboses among 1500 cases of the disease.

*Significance of cancer.* The significance of malignant neoplasms as predisposing factors has also been emphasized. Trousseau<sup>67</sup> was one of the first to call attention to the causal relation of cancer and thrombosis and to note that frequently the first manifestation of an internal cancer is peripheral phlebitis. Sproul<sup>68</sup> noted the relatively high incidence of venous thrombosis as a complication of carcinomas of the body or the tail of the pancreas. In 56 per cent of cases of carcinoma of these portions of the pancreas, a single thrombus was present, whereas in 31 per cent the venous thrombosis was largely disseminated. Flörcken<sup>21</sup> and Schäfer<sup>69</sup> have also emphasized the effect of carcinoma as an etiologic factor. In patients with cancer, because of the tendency toward thrombosis, it is essential to use prophylactic measures. In the absence of specific preventive measures, compression of the extremities by means of elastic adhesive is of great value.

*Hydration and mineralization.* The replacement of fluid as a preoperative measure is imperative

because dehydration and increased viscosity of blood predispose to thrombosis. As emphasized by Gordon-Watson,<sup>70</sup> it is essential to replenish the fluids in those patients who have had purgation preoperatively and who have lost considerable fluid by hemorrhage, sweating or vomiting. Preoperative remineralization is of equal value. Kopf<sup>71</sup> is of the opinion that the highly purified sodium chloride employed at present is responsible for the high incidence of thrombosis. He believes that a great deal can be accomplished in the preparation of these patients by giving various salts beforehand, such as mineral water, Brunner's salts and Glauber's salts. Ross<sup>72</sup> found in experimental animals that following the administration of small amounts of calcium nitrate there was an increased tendency to thrombosis because of the alteration in the calcium-sodium ratio. Russo<sup>73</sup> attempted to determine whether there is a sodium chloride deficiency in thrombosis. He investigated 44 cases either at the time of or shortly after the occurrence of a venous thrombosis. Of these, 8 patients had thrombosis of both lower extremities; 10, pulmonary infarction; 21, marked cardiac insufficiency; and 2, postpartum thrombosis. The sodium chloride values of the blood serum in 10 cases fluctuated between 500 and 550 mg.; in 28, between 550 and 600 mg.; and in 6, between 600 and 620 mg. per 100 cc. On the basis of these results, Russo concludes that hypochloremia is not a factor in the production of thrombosis. These conclusions are supported by the contentions of Vogt,<sup>26</sup> who believes that a salt-free diet is of prophylactic value. On the other hand, Menninger-Lerchenthal<sup>74</sup> is of the opinion that a hypochloremia is a factor in thrombosis. He reports 5 cases of spontaneous thrombosis or thrombophlebitis in patients who received varying doses of sodium bromide and who were on a low-salt diet. He thinks that the administration of bromides results in displacement of the chloride radicle, which according to him and to Prima<sup>75</sup> exerts a detoxifying action. These authors are of the opinion that postoperative hypochloremia is a factor in the development of thrombosis. Prima has given 400 to 1000 cc. of physiologic saline solution to all patients postoperatively, and during a period of thirteen years has never seen any thrombosis. It is evident that hydration and remineralization are useful measures in the prevention of thromboembolism.

*Correction of anemia and other dyscrasias.* It is essential preoperatively to correct an existing anemia, because of the increased tendency to thrombosis in such a condition. Lockhart-Mummery<sup>76</sup> and Donald,<sup>77</sup> in 1924, directed attention to the

greater likelihood of thrombosis in anemia. The latter reported 3 cases of profound anemia in which the patients developed fatal pulmonary embolisms, and believed that the thrombosis was to a large extent caused by the anemia. Others<sup>78, 79</sup> have also emphasized the increased incidence of thrombosis in patients with long-continued hemorrhage. Drinker, Drinker and Kreutzmann<sup>80</sup> demonstrated that following hemorrhage there is an increase in the cellular elements, which may increase the coagulability of the blood. These changes may be at least partly responsible for the increased incidence of intravenous clotting in cases of anemia secondary to hemorrhage. In addition to the increased coagulability of blood, anemia also predisposes to thrombosis because of its secondary effect on the cardiovascular system, resulting in diminution in cardiac tone, and circulatory retardation. Because anemia is an important predisposing factor in thromboembolism, careful blood studies must be made preoperatively in all cases, and deficiencies should be corrected by blood transfusions and other appropriate measures. Polycythemia is not infrequently complicated by intravascular clotting, particularly in the portal vein, probably because of the increased viscosity of the blood resulting from the increased number of erythrocytes. In such cases, it is desirable to employ venesection preoperatively.

Whereas intravenous clotting can occur in any patient, it is particularly likely to occur in the presence of the predisposing factors discussed above. Accordingly, it is essential that such factors be recognized preoperatively, that appropriate prophylactic measures may be instituted. Obviously, in some cases, the prophylactic measures that can be used are specific, such as correction of cardiovascular disturbances, whereas in others the preventive measures are necessarily nonspecific.

### *Operative Procedures*

*Atraumatic surgery.* As emphasized previously,<sup>1-4</sup> and as mentioned above, the absorption into the vascular system of proteid disintegration products originating from injured tissue, as a result of operative, accidental or puerperal trauma, infection and invasion by cancer, increases the coagulability of the blood and predisposes to intravascular clotting. The role of accidental trauma is emphasized by McCartney's<sup>81</sup> statistics. In 73 cases of pulmonary embolism there were 15 which were strictly post-traumatic; in 12 of the latter the patients had fractures of the lower extremity, and in all, the patients were confined to bed. Potts<sup>82</sup> reported 95 cases with fractures of the lower extremity, in 5 of which the patients

developed thrombophlebitis; he is of the opinion that thrombophlebitis developed in these cases partly because the extremity was immobilized and the patient was unable to take exercises.

Whereas it is impossible to control the degree of accidental trauma and difficult, if at all possible, to control the injury to tissue by infection and neoplastic disease, a great deal can be accomplished operatively by employing atraumatic surgery. As has been repeatedly stressed, *sharp dissection* results in less trauma than blunt dissection. The *gentle handling of tissues* cannot be overemphasized. The clamping of vessels only and the avoidance of mass grasping of tissue are essential. The significance of operative trauma in the production of postoperative thrombosis has been emphasized by a number of clinical and experimental observations.<sup>24, 29, 70, 76, 78, 83-85</sup> Lambret and Driesens<sup>80</sup> found that following an operation there was a rise in the polypeptides, which reached its maximum about the fifth day, and that this was more prolonged the more traumatic and the more histolytic the operative procedure. Mason<sup>81</sup> and Takaura<sup>82</sup> have shown that tissue extracts are potent in the production of intravascular clotting, the former investigator having found that 0.003 gm. of lung-tissue extract will produce complete intravascular coagulation in a rabbit. Of equal importance is the *absolute hemostasis*, because the absorption of blood from a wound gives rise to proteid disintegration products. Because absorbable suture material produces an intense inflammatory reaction, which is necessary for proteolytic digestion of the suture, greater tissue injury occurs in wounds closed with such material, a condition that increases the absorption of split-protein products. If *fine nonabsorbable suture material* is used, this reaction of the wound is definitely decreased, as evidenced by the clinical appearance of the wound and by a much lower temperature curve. This is further supported by the histologic examination of experimentally produced wounds.<sup>93</sup> In our clinic, we have for the past two years used cotton suture material exclusively, because it was found experimentally that this material gave the least reaction of all those investigated.

**Avoidance of contamination.** It is imperative that the trauma during the operation be reduced to a minimum, and that contamination of the wound be prevented, not only because the infection itself is undesirable, but also because of its effect on intravascular clotting. The continuation of the infection with the destruction of tissue, causing the liberation of larger quantities of split proteins, favors thrombosis.

**Hydration and mineralization.** During the op-

erative procedure, it is essential that excessive loss of fluid be prevented. Commonly, under a general anesthetic, there is considerable loss of fluid through perspiration and insensibly through the lungs. Because dehydration and loss of electrolytes predispose to thrombosis, fluids should be administered parenterally, either intravenously or subcutaneously, during the operation. The importance of the fluid loss during an operative procedure has repeatedly been emphasized by Collier and his associates.<sup>94, 95</sup>

**Prevention of circulatory collapse.** Patients who are submitted to extensive operative procedures with considerable trauma, particularly if there is much loss of blood, may develop a circulatory collapse. In such cases, it is imperative to prevent this collapse by the prophylactic administration of saline solution, blood or plasma. It may be necessary to resort to vasoconstrictor drugs, to prevent the prolongation of a hypotension, which would predispose to intravascular clotting. The prevention of circulatory collapse, owing to its effect on intravascular clotting, is of value because such collapse favors vascular retardation, anoxia and injury to the vascular endothelium and, if prolonged, increases the blood viscosity.<sup>96</sup>

**Avoidance of chilling.** Chilling during and after the operation should be prevented because of its vasoconstrictor effect, which predisposes to vascular retardation. Chilling is probably detrimental in another way, since it increases the viscosity of the blood, as shown by Barbour and Hamilton,<sup>97</sup> who demonstrated that exposure to cold causes a loss of fluid from the vascular channels into the tissues. This increases the viscosity and the clotting tendency, and is probably the effect of a combined sympatoadrenal activity. The necessity of preventing chilling during the operative procedure has been emphasized by Leriche<sup>98</sup> and others,<sup>99, 100</sup> who employed infrared irradiation during the course of an operation. Birgus<sup>101</sup> suggested the use of flannel stockings during the operative procedure to prevent chilling. This is an extremely valuable suggestion, and stockings should be applied to the lower extremities during not only the operation but also the postoperative period.

#### Postoperative Procedures

**Hydration and mineralization.** After a patient has been returned to his bed following an operative procedure, it is imperative that the replacement of fluids and electrolytes be continued, because in the early postoperative period, particularly after laparotomy, the patient is unable to take fluids by mouth and frequently is losing considerable fluid from his stomach and intestine as



a result of vomiting or removal by means of an indwelling duodenal catheter. An increased viscosity of the blood may occur postoperatively, as demonstrated by Zarubin<sup>102</sup> and Bolognesi.<sup>103</sup> Similar observations were made by Löhr and Löhr,<sup>104</sup> who found that the viscosity parallels the erythrocytic sedimentation rate. In addition to the reasons mentioned above for the administration of fluids and electrolytes, it is essential that the water balance be re-established as quickly as possible, because in this way the elimination of waste products, among which are the split-protein substances that predispose to intravascular clotting, is effected.

**Posture.** The posture of the patient postoperatively is of great importance in predisposing to or preventing thrombosis. Because vascular retardation is a prominent precipitating factor in the production of intravascular clotting, postures that cause slowing of the blood stream should be avoided, and conversely, postures that favor the return flow of blood in the venous system should be used. The placing of a patient in a Fowler's position, with flexion of the thighs on the abdomen and flexion of the legs on the thighs at the knees, results in compression of the vessels in the popliteal space and should therefore be avoided. Whereas flexion of the thigh on the trunk theoretically produces compression of the femoroiliac veins beneath the inguinal ligament, Friedländer<sup>42</sup> has shown that such a position actually produces less compression, favors the return flow of blood, and tends to prevent vascular retardation. This may be accomplished either by elevating the foot of the bed from 30 to 45 cm. or, preferably, by elevation of the leg and foot and flexion of the thigh on the trunk at an angle of 45°. Friedländer showed that, if the thigh is extended and on a level with the trunk, the femoroiliac veins are kinked as they pass from the thigh through the inguinal canals down into the pelvis, and that the veins assume a straight direction if the thigh is flexed on the trunk at an angle of 45°. He also emphasizes the value of elevating the leg above the level of the thigh so that no kinking occurs in the popliteal space. Elevation of the foot of the bed to prevent vascular retardation, a procedure that we believe should be employed, has been repeatedly emphasized.<sup>18, 22, 42, 101, 105-113</sup> Frykholm<sup>114, 115</sup> and Patey<sup>116</sup> advocate elevation of the head of the bed as a prophylactic measure in intravascular clotting. Frykholm is of the opinion that if the lower extremities are elevated, the deep veins become emptied of their blood and the venous endothelium suffers, because lack of nutrition causes changes that favor thrombosis. On

the other hand, if the patient is placed in a head-up position, these veins become filled, the vascular endothelium is better nourished, and there is less danger of change in the endothelium and resultant thrombosis. Patey believes that the contraction of the muscles necessary to keep the patient in this position favors the movement of blood, a factor that cannot be denied, and that if thrombosis does occur, it will take place in a vessel that is dilated and in which a greater inflammatory reaction and a more extensive clot will result, tending to fix the thrombus in the vessel. Whereas muscular contractions are necessary to keep the patient in the head-up position and are of undoubted benefit, it is our firm conviction that better results are obtained by elevation and mobilization of the extremities, which speed up the blood flow and prevent circulatory retardation.

**Mobilization.** The immobility of a patient postoperatively is undesirable for several reasons. As a result of the quiescence, cardiovascular activity is decreased, which tends to produce vascular retardation. Muscular inactivity predisposes to vascular stasis because the movement of blood in the vein is dependent to a great extent on the contraction of muscles. For these reasons, early postoperative mobilization is essential as a prophylactic measure in venous thrombosis. Ries,<sup>117</sup> Richardson,<sup>118</sup> Boldt<sup>119</sup> and others<sup>120-125</sup> were early advocates of movement of the legs while the patient is in bed. More recently, the significance of such exercise has been further emphasized.<sup>1-4, 27, 78, 82, 105, 126-136</sup> Although the bed bicycle of Gamble<sup>137</sup> and the elaborate mass gymnastic procedures recommended by Kirschner,<sup>138</sup> which consist in performing co-ordinated exercises twice daily with music under the supervision of a gymnast, are probably unnecessary, movement of the muscles of the lower extremities, preferably against a resistance, should be used in all cases when possible. Potts<sup>82</sup> has emphasized that whereas thrombosis and embolism are common in patients with fractures who are confined to bed and in plaster encasements, they are rare in ambulatory patients with arm, leg, shoulder or spine fractures, in similar encasement. In each case, the amount of tissue trauma and the local immobility are the same, the only difference being the systemic immobility in the former and the systemic mobility in the latter. The value of local and systemic immobilization is further stressed by McCartney's<sup>81</sup> 73 cases of pulmonary embolism, of which 15 were strictly post-traumatic; 12 of these patients had lower-extremity fractures and were confined to bed. That exercises alone will not prevent intravascular clotting, however, is exemplified by a case of Conner's in which

rather extensive thrombosis occurred in a patient with typhoid fever who conscientiously used daily exercises of his arms and legs.

*Early ambulation.* Early ambulation of the patient postoperatively is favored in most Continental clinics. Not infrequently, a patient who has had an appendectomy performed through a muscle-splitting incision under local analgesia is permitted to walk back to his room. Campeanu<sup>139</sup> reported 1300 cases, many of which were severe, in which the patients were allowed to walk directly from the operating room to the ward and to take gymnastic exercises immediately afterward, including even jumping. Campeanu has extended early ambulation to such an enthusiastically ludicrous degree that he performed an appendectomy on one of his assistants, who immediately afterward assisted him in another operation, and also on another assistant, who immediately afterward performed an appendectomy. Patients who have had extensive operations, such as resection of the stomach, are allowed to sit on the edge of the bed on the afternoon of the operation, and to sit out of the bed the day following the operation. This ambulation is used for two reasons: to decrease the circulatory retardation, and to diminish the incidence of respiratory infection. Zava<sup>140</sup> quotes his experience with this therapy in more than 6000 operations without a single case of embolism, although many of the cases were gynecologic or other pelvic procedures. He gets his patients up either on the first or second day, and, if this is not possible, he keeps them in bed until the second week, because he quotes Forgue as stating that embolism is likeliest to occur between the third and thirteenth days. The value of early ambulation is emphasized by von Jaschke,<sup>22</sup> who found that among 300 cases in which patients were allowed to get up relatively late, there were 2 per cent thromboses and 1 per cent fatal emboli, whereas in 387 cases in which early ambulation was used, the incidence of thromboses was 0.5 per cent and there were no fatal emboli. In the Essinger University Clinic, there were, from 1906 to 1912, operations on 1504 cases, following which the patients got up at the end of the second week and in which the incidences of thrombosis and fatal embolism were 2.63 and 1.40 per cent, respectively. From 1912 to 1918, there were operations on 2053 cases, following which patients got out of bed between the second and fifth days and in which the corresponding incidences were 1.75 and 0.6 per cent. Smith<sup>141</sup> reports abdominal or pelvic operations following which the patients have got out of bed within a few days. There were four deaths in the group, one of which

was due to embolism; none of the cases could be attributed to the early rising. Voegt<sup>135</sup> and von Jaschke<sup>22</sup> are other advocates of early ambulation. The advantage of getting the patient out of bed relatively early is exemplified by the investigations of Smith and Allen,<sup>142</sup> in which it was shown that postoperatively beginning on the fifth day the circulation time was increased and that on the tenth day it was approximately 50 per cent greater than the preoperative average. Eighty-two per cent of the individual cases showed increases of four or more seconds at some time after the operation. Similar observations were made by Sylvan.<sup>32</sup>

*Respiratory stimulation.* Normally, the negative pressure within the thorax favors the return of venous blood to the cardiac chambers. Because of the diminished respiratory activity that follows operation, there is an interference with the normal venous return. Moreover, hypopnea occurs postoperatively as a result of pain caused by movement of the abdominal muscles and an increase in abdominal tension. It has been shown repeatedly that postoperatively the diaphragmatic excursions are diminished, which results in concomitant diminution in the negative intrapleural pressure, venous stasis and circulatory retardation.<sup>143-152</sup> Prevention of hypopnea is therefore important, and patients should be instructed to take frequent deep breaths during their waking hours. It is the custom in our clinic to have the patient take at least ten deep breaths every hour. Whereas it is frequently necessary to insist on voluntary deep breathing, which is preferable, if this is not possible it may be necessary to employ carbon dioxide inhalations.<sup>153 157 158</sup> Because of the depressant effect of opiates on the respiratory center, it is desirable to use them as sparingly as possible, to minimize the danger of hypopnea. The value of deep breathing has been repeatedly emphasized.<sup>19 20 78 82 93 101 105 116 122 123 131 134 135 154 155</sup>

*Abdominal tension.* Increased intra-abdominal pressure also favors circulatory retardation by exerting pressure on the intra-abdominal veins, and thus interfering with the return flow of venous blood from the lower extremities. Increased intra-abdominal tension may result from a number of factors, such as application of constricting bandages, which are frequently used by surgeons in an attempt to give support to the abdominal wall, and functional inactivity of the gastrointestinal tract, with its associated accumulation of fluid and gas in the stomach and the intestine (ileus). For this reason, the increased intra-abdominal tension resulting from tight bandages or from ileus should

be combated by avoidance of tight dressings, by the use of appropriate devices, such as the indwelling catheter and the double tube, and by other methods previously described.<sup>156</sup> As shown by Pat-ey<sup>116, 161</sup> and Frimann-Dahl,<sup>147</sup> there is a definite increased intra-abdominal tension postoperatively, apparently the result of a decreased action of the diaphragm and the splinting of the abdominal wall.

*Compression bandages.* In patients in whom an intravenous clotting is likely to occur the application of compression bandages to both lower extremities should be used postoperatively for the same reasons advocated for their preoperative use, given above.

*Heat.* The application of heat in the form of a heat tent to the lower part of the abdomen and the extremities is undoubtedly of value after an operation, not only because of its beneficial effect on the tone of the intestine, but also because it produces reflex vasodilatation of the peripheral vessels. The extremely low incidence of intravascular clotting in our clinic is owing, we believe, to the fact that large heat tents covering the abdomen and lower extremities are routinely used postoperatively. The application of heat is particularly important, because circulatory activity is further decreased by the peripheral vasoconstriction that has been shown to exist by Leriche<sup>98</sup> and Kvale,<sup>157</sup> and in previous investigations by us. Because of the vasoconstriction of the capillary bed, venous stasis occurs, which in turn predisposes to thrombosis. Smith and Allen<sup>142</sup> showed that postoperatively the circulation was definitely slowed and that this was more pronounced when the extremity was cold and less marked when it was hot, irrespective of the cause of vasodilatation. The use of woolen or flannel stockings postoperatively, to retain the body heat and prevent irradiation, cooling and vasoconstriction, is desirable.

*Hirudinization and heparinization.* The use of anticoagulants as prophylactic measures has become increasingly popular. Hirudinization and heparinization owe their efficacy to their anticoagulant activity. The former has been emphasized by one of us in collaboration with Mahorner,<sup>158</sup> and more recently by Chalié,<sup>159</sup> and Rouhier.<sup>160</sup> Murray and Best and their co-workers<sup>161-163</sup> in Canada, Crafoord<sup>164, 165</sup> in Sweden, and Priestley, Essex and Barker<sup>166</sup> in this country have used heparin prophylactically to prevent thromboembolic phenomena. These investigators found experimentally that by administering purified heparin intravenously over a period of hours it was possible to diminish the coagulation time considerably. Good results have been reported from its clinical use. Murray and Best<sup>161-163</sup> used

heparin postoperatively in 315 cases, and in none did thromboembolism develop. Crafoord<sup>164, 165</sup> treated 126 cases prophylactically with heparin one developed a pyrexia, which might have been due to thrombosis. In a control group of 80 cases, 122 patients (15 per cent) had evidence of thromboembolism, although in 64 of these the only manifestations of thrombosis were changes in temperature and pulse. Sodium citrate intravenously has been suggested by Kreiner<sup>167</sup> and others<sup>12</sup> as another prophylactic anticoagulant. Unless there is definite evidence of hereditary predisposition or unless the patient gives a history of having had previous thromboses, it is doubtful whether the routine use of any of these anticoagulants is justified prophylactically.

#### THERAPEUTIC MEASURES

By the institution of the above prophylactic measures, most cases of intravascular clotting can be prevented, and this without doubt is a desideratum. Occasionally, in spite of the use of these procedures, intravascular clotting occurs. The prognosis and the therapy in each case are dependent on the type of the lesion and its location. Of great significance is the differentiation between intravascular clotting in the superficial and in the deep veins, and of even greater importance is the distinction between intravascular coagulation associated with an inflammatory lesion of the vein, that is, thrombophlebitis, and coagulation in which there is no associated inflammatory process, that is, phlebothrombosis. Generally, the prognosis is better, and the therapy more easily applied in cases with superficial thrombosis than in those with thrombosis of the deep veins.

##### *Superficial Thrombosis*

*Thrombophlebitis.* In cases of thrombophlebitis involving the superficial veins, the treatment is usually *conservative* and consists in compression of the entire extremity from the metatarsal phalangeal joints up to the groin. Adhesive elastic bandages should be applied to the thigh because of the difficulty of preventing the ordinary type of compression bandage from slipping owing to the conical shape of the thigh. To prevent propagation of a thrombus, it is imperative that these patients be treated by ambulation and not be allowed to remain in bed. The value of the compression and ambulation therapy was first emphasized by Fischer.<sup>40</sup> Compression of the extremity is efficacious by compressing the vein wall against the thrombus, tending to fix it, and by producing relative immobility of the vein.

Whereas thrombophlebitis in the superficial veins can usually be treated satisfactorily by compression and ambulation, *radical therapy*—high

ligation—is occasionally desirable. In the majority of superficial thrombophlebitides, radical therapy is unnecessary; however, because of the occasional detachment of a superficial thrombus resulting in massive embolism, this procedure becomes lifesaving. We have observed 4 cases at autopsy in which death resulted from a massive pulmonary embolism, the clot originating in the long saphenous vein. These fatalities could have been prevented by the timely ligation of the saphenous at its junction with the femoral vein. Homans<sup>168</sup> states that he has observed infarction but never fatal pulmonary embolism following thrombophlebitis of varicosities. We believe that in cases with long-saphenous-vein involvement in which the thrombophlebitic process has extended up to the lower part of the thigh, it is desirable to do a high ligation at its junction with the femoral vein and to follow this by compression and ambulation. Approximately forty-five years ago, Gluck<sup>169</sup> reported a case of postpuerperal thrombophlebitis of the long saphenous vein successfully treated by proximal ligation. In 1909, Müller<sup>170</sup> reported a similar case. Homans<sup>168</sup> advocates high ligation of the long saphenous vein when it is involved in a thrombophlebitic process. Hollingsworth<sup>171</sup> has recently reported a case in which this was done. Occasionally in varicosities, particularly those involving the leg at the site of a hugely dilated vein, localized thrombophlebitis occurs. This is extremely painful and may result in an ulceration, owing to interference with the blood supply. In such cases, local excision of the thrombophlebitic segment is desirable. When suppuration occurs in the thrombophlebitic segment, high ligation of the saphenous should be performed because of the possible propagation of the thrombus and detachment of infected emboli. Occasionally, excision of a localized thrombophlebitic segment of vein is desirable when an intraluminal suppuration occurs. Generally, however, because the suppurative process extends beyond the vein, in addition to high ligation of the main stem of the superficial vein, incision and drainage of the involved areas are necessary. Büdinger<sup>172</sup> advocated multiple incisions along the course of the involved veins in suppurative superficial thrombophlebitis. Eisenklam, a student of Büdinger, recently reported the results in 66 cases of nonsuppurative and suppurative superficial thrombophlebitis. Forty-two patients so treated were discharged from the hospital on the seventh or eighth day. In one of our cases, incision and drainage of a local suppurative thrombophlebitic process resulted in prompt cure. In another with propagation and evidence of sepsis, high ligation was necessary and was followed by recovery. In

a third with a rapidly progressing suppurative thrombophlebitis and sepsis, as evidenced by positive blood cultures, high ligation and subsequent incisions and drainages were necessary to effect a cure.

**Phlebothrombosis.** Thrombophlebitis of the superficial veins can be readily recognized not only by the presence of the palpable clot in the vein but also by local manifestations of inflammatory reaction, namely, tenderness, redness and increased heat over the involved vein. On the other hand, intravascular clotting unassociated with an inflammatory reaction, phlebothrombosis, occurs with evidence of minimal inflammatory reaction, the principal manifestation being a palpable clot in the vein. As mentioned before, the danger of such a clot's becoming detached, and thus gaining entrance to the venous system and being carried to the pulmonary veins, is particularly great. It is for this reason that these patients should never be treated conservatively, but high ligation of the vein at its junction with the deep venous system should be done as early as possible, the extremity compressed by means of bandages, and the patient made ambulatory. This relatively simple procedure will not only shorten the patient's convalescence but will in many cases prevent tragic complications resulting from the detachment of the nonadherent clot.

#### *Deep Thrombosis*

Intravascular clotting of the deep veins produces a different clinical picture from that of the superficial veins, and here again one must distinguish between thrombophlebitis and phlebothrombosis.

**Thrombophlebitis.** In cases in which there is an inflammatory involvement of the vein with accompanying systemic manifestations of infection, such as fever and leukocytosis, there is generally a decrease in the surface temperature of the involved extremity, a paradoxical manifestation. This is in contrast to the thrombophlebitic lesions involving the superficial veins in which the skin overlying the vein is red and warm. It has been well known for years that the involved extremity of patients with deep thrombophlebitis, particularly in the femoroliac veins, in addition to being swollen, is white and frequently has a cyanotic hue as well as a decrease in the surface temperature. The significance of this paradoxical manifestation, that is, coldness and pallor in the area of involvement in the presence of inflammation and pyrexia, was not appreciated by us until it became apparent by our animal and clinical investigations that, although the lesion was primarily in the large, deep veins, the manifestations were principally those of spasm of the arterial system, the decrease in tem-

perature and the whiteness of the extremity being due to ischemia.

The treatment of thrombophlebitis of the deep veins can be divided into two large categories, *conservative therapy* and radical therapy. In most cases, the former suffices. Elevation of the extremity should be carried on because it favors the return flow of blood and tends to decrease the propagation of the thrombus. Whereas immobilization previously has been considered an important form of therapy,<sup>34, 87, 113, 126, 129, 131, 174-185</sup> we are of the opinion that absolute immobilization is undesirable. Of great value in conservative therapy is the application of compression bandages to the extremity. The bandages should extend from the toes to the inguinal region. The rationale for their use has been discussed above, but briefly depends on an increased flow of blood in deep veins. Of equal significance is the beneficial effect they exert in preventing edema, and in retaining heat and increasing the vascularity of the extremity by virtue of the fact that they encase it. Müller<sup>43</sup> advocates the use of compression bandages and getting the patient up as soon as possible. He reports 85 cases of deep thromboses treated in this way. Many of the patients had massive swelling; some had pulmonary infarcts and had been in bed for weeks. Usually, after ten to fourteen days all symptoms had disappeared. In none of these cases did small lung infarcts develop, but there were two fatal pulmonary emboli, which the author believes cannot be blamed on the use of the compression bandage. In contrast, 40 cases of thrombophlebitis were treated by elevation only. In this group there were 6 cases (15 per cent) of fatal pulmonary embolism. There were 3 additional cases of pulmonary infarction. Müller states that compression treatment has decreased the incidence of fatal embolism from 15 to 2.3 per cent. He believes that compression re-establishes the competence of the venous valves and favors the attachment of the thrombus to the vein wall. He also thinks that by improving the circulation it prevents the propagation of a thrombus, which because of lack of attachment may be easily broken off and result in embolism. This is the most dangerous feature of thrombophlebitis. In his experience, the use of the compression bandage decreased the convalescent time from six to eight weeks to eight to twelve days. Fischer<sup>40</sup> has used this method of therapy in several thousand cases, and has never observed fatal embolism. Krammer<sup>186</sup> and Friedländer<sup>41</sup> treated a series of 196 cases by compression bandage, with only 1 case of fatal pulmonary embolism, which they thought was due to incorrect bandaging. On the

other hand, in 308 cases treated by elevation there were 64 cases (16 per cent) with fatal emboli.

Bahls<sup>187</sup> states that since 1923 in the Kappis Clinic they have used compression bandages in cases of thrombosis and thrombophlebitis. Of 181 cases of thrombosis, they have lost 6 patients from emboli. Three of these would have died anyway. He states that if the bandage is applied at the earliest manifestation of thrombosis, fatal pulmonary embolism does not occur. In cases of thrombophlebitis, he advocates the application of adhesive bandage and ambulation. Lepler<sup>23</sup> treated 45 cases of postoperative thrombosis by means of adhesive plaster compression, and of this number 35 patients had no complications, 9 developed infarcts, and 1 died of pulmonary embolism. There were 36 cases with progressive thrombosis and thrombophlebitis treated in this way, in none of which complications occurred. In 17 cases of pulmonary infarction with no evidence of thrombosis, adhesive compression of the extremities was used prophylactically; of these, 3 patients developed fatal pulmonary emboli. Lepler<sup>23</sup> emphasizes that in the cases treated by adhesive compression in which ambulation was possible neither infarction nor fatal embolism developed, whereas infarction occurred in 9 and fatal pulmonary embolism in 4 patients who were bedridden in his series.

Cabernard<sup>188</sup> states that he used compression therapy in thrombosis and thrombophlebitis for five or six years in more than 100 cases and never observed infarcts or emboli. Whereas, previously, patients with thrombophlebitis had been kept in bed for six weeks, in this group they remained in bed only four or five days. Of about 40 cases with fever, 1 patient remained in bed for three weeks, 1 for fourteen days, and 2 for ten days. In the last 3 patients, the thrombophlebitis extended above the inguinal ligament. The other patients stayed in bed only two or three days. When the condition of the patient permitted, ambulation was begun on the day the bandage was applied. Numerous other observers are warm advocates of the use of compression bandages.<sup>18, 21, 26, 27, 36, 37, 113, 189-193</sup>

The application of heat postoperatively is of advantage in thrombophlebitis of the deep veins, as well as that in superficial veins. This has been adequately discussed above. Similarly, the use of anticoagulants, such as hirudin and heparin, may be of value in isolated cases. Termier,<sup>194</sup> in 1922, is credited with the revival of treatment of thrombophlebitis by leeches. He reported 73 cases in which this form of therapy was used with remarkable relief of acute manifestations. Subse-

quently, numerous others, especially in Europe, reported similar observations following this method of therapy.<sup>21, 22, 35, 38, 188, 189, 195-225</sup> Hirudin, which is secreted by the leech's salivary gland, can completely prevent coagulation, and in vitro has been observed to cause dissolution of a blood clot. It was on this basis that Termier<sup>191</sup> explained the good results obtained by the use of leeches. Other explanations are based on the production of an increase in phagocytic and bactericidal powers,<sup>229</sup> local blood letting,<sup>223</sup> prevention of venous spasm<sup>205</sup> and general hirudinization.<sup>230</sup> The action of hirudin was experimentally investigated in the Tulane Surgical Laboratory, and leeches were used clinically.<sup>188, 231</sup> There was a rapid subsidence of symptoms following this procedure. At present, its greatest value lies in the treatment of such conditions as portal thrombophlebitis (pyelophlebitis). Some observers<sup>160, 232, 233</sup> have warned against the use of hirudin on the basis that it might produce a liquefaction of the clot, with resulting embolism; this has never occurred in our experience.

Although the use of heparin is of no value, so far as the clot that is already formed is concerned, it is of value in preventing the propagation of a thrombus by decreasing the coagulability of the blood. Murray and Best<sup>161, 162</sup> heparinized 7 patients with pulmonary embolism and infarcts, with recovery in all. Of 28 cases of thrombophlebitis treated with heparin, none developed emboli. Crafoord,<sup>164, 165</sup> on the other hand, did not obtain such favorable results in a similarly small series. Of 20 cases with thromboembolic manifestations, there were only 5 in which the results were good. More recently, Murray<sup>234, 235</sup> reported 81 cases of phlebitis in which heparinization was used. The results in this group were very good, and no patient had pulmonary embolism. He is at a loss to explain satisfactorily these beneficial effects; he states: "The only effect that heparin could have is to prevent extension of thrombosis. It is possible, therefore, that the healing of the lesion already present is allowed to take place and that with prevention of extension of the process the active inflammation recedes and the symptoms disappear with it." The heparin is administered by continuous intravenous injection, and the dosage is regulated so that the clotting time of the blood is maintained at between fifteen and twenty minutes. The patient is kept in bed on the average of one week, and after the acute manifestations have subsided,—by the third or fourth day,—active exercises in bed are encouraged. At the end of this time, he is allowed out of bed, and if no untoward manifestations

develop the administration of heparin is discontinued. Murray and Best state that most of their patients were discharged from six to fourteen days after treatment was instituted.

Graves,<sup>236</sup> in 1906, reported 2 cases of thrombophlebitis of varicosities that were successfully treated with irradiation. More recently, Henschen and Becker<sup>237</sup> advocated roentgen irradiation in thrombophlebitis. They state that from four to twelve irradiations effect a disappearance of the phlebitic symptoms. They advise the use of between 100 and 200 r, applied over the involved extremity, and emphasize that the severer the inflammation the weaker the irradiation should be. They also state that the dose should be decreased or increased according to the location, the type of infection, the age and the general condition of the patient. They believe that the beneficial results are due to the increase in the bactericidal action of the blood stimulation of the reticulo-endothelial system and to the formation of antibodies. They state that the convalescence is definitely shortened. Birgus<sup>101</sup> reports the use of roentgen irradiation in 49 cases of thrombosis, 23 of which were deep, 20 superficial and 6 mixed. The extremity was irradiated over several fields, the dosage varying from 100 to 200 r per field. In superficial processes, one treatment was usually enough. In the acute processes, the treatment was begun with small doses. Birgus states that the duration of the process is shortened by roentgen-ray treatment, the pain and swelling disappear more rapidly, and the pulse and temperature soon return to normal. Halban<sup>238</sup> and Kilbourne<sup>190</sup> advocate using deep x-ray therapy in chronic thrombophlebitis. The latter author emphasizes that roentgen-ray therapy should not be used until the thrombophlebitic process has become chronic.

In previous experimental and clinical investigations, we<sup>1-4</sup> have shown that vasoconstriction of the arterioles and venules plays an important role in producing a persistence of clinical manifestations. The use of vasodilatory measures in the treatment of thrombophlebitis has recently received considerable attention. Murphy<sup>239</sup> and, more recently, Sokolov and Meyers<sup>240</sup> have advocated iontophoresis with acetyl-beta-methyl-choline hydrochloride (Mecholyl). Murphy reported favorable results with his form of therapy in 33 cases of thrombophlebitis. Nineteen patients with thrombophlebitis of the deep veins were treated by this method by Sokolov and Meyers, and improvement was observed in 18. However, only 3 were in the acute stages, although the authors stated that the best improvement was obtained in cases of acute involvement. Vasodilatation by

means of artificially induced fever has been suggested by Weymeersch and Snoeck<sup>241</sup> and by Pitfield.<sup>242, 243</sup> The former authors used injections of sterile milk to produce the fever, and the latter employed injections of typhoid vaccine. Paine and Levitt<sup>244</sup> have recently reported the use of intermittent venous occlusion in the treatment of thrombophlebitis. This method of therapy was employed in 4 cases of acute thrombophlebitis, and in 7 of the chronic form, with relief of pain, tenderness and discomfort. Edema was decreased in some cases but unaffected in others.

In our experience, the best method of therapy in thrombophlebitis of the deep veins is the production of vasodilatation by blocking the regional sympathetic ganglion with procaine hydrochloride, as suggested by Leriche.<sup>245, 246</sup> In 1934, Leriche and Kunlin<sup>247</sup> reported 3 cases of acute postoperative phlebitis successfully treated by this method, and subsequently they<sup>248</sup> reported other cases in which similar results were obtained. Since then, numerous other reports<sup>249-260</sup> have appeared, which attest to the success of this method of therapy.

We<sup>1-4</sup> have shown by experimental and clinical observations that vasospasm resulting from impulses originating in involved venous segments is one of the most important factors in the production of the clinical manifestations of thrombophlebitis. These investigations indicate that the vasospastic influences affect both arterioles and venules. In animal experiments,<sup>261, 262</sup> the volume pulsation in the hind feet of dogs was determined plethysmographically by the sensitive method of Turner. The femoral veins of the dogs were exposed from just proximal to the saphenous entrance below to Poupart's ligament above, and ligatures were placed at these two sites. A chemical thrombophlebitis was produced in the ligated venous segment by injecting a 40 per cent aqueous solution of sodium salicylate. The perivascular tissues in the entire venous segment were then carefully infiltrated with procaine hydrochloride solution, and plethysmographic determinations were made following each of these procedures. In another group of animals, a similar experiment was performed, except that a resection of the corresponding lumbar sympathetic ganglia and intervening chain had been performed twenty-four hours previously. It was invariably found that the volume of pulsation in the foot was markedly decreased following ligation of the femoral vein, and that it almost disappeared following the production of the chemical thrombophlebitis. This effect was always abolished by the interruption of nerve pathways by local infiltration with procaine hydrochloride at the site of the chemical irritation or by resec-

tion of the lumbar sympathetic ganglia and the intervening chain. These experiments demonstrate that the decrease in volume pulsation following chemical thrombophlebitis and periphlebitis is due to vasoconstrictor impulses initiated locally by the chemical irritant and coursing through the sympathetic ganglia to reach the terminal arterial vessels of the extremities. We have also been able to demonstrate clinically that a definite vasospasm exists in thrombophlebitis and that this vasospastic action can be abolished by novocain block of the regional sympathetics. Numerous other clinicians have shown that a localized thrombophlebitic process can initiate a marked vasospasm.<sup>263-284</sup> Indeed, the vasospasm may be so great that the condition appears to be arterial embolism,<sup>257, 264, 266, 271-278, 280-283, 285-290</sup> and in some cases actual gangrene has occurred.<sup>285, 287, 289, 291-294</sup>

In previous publications, we<sup>1-4</sup> have discussed in detail the mechanism by which vasospasm and thrombophlebitis can produce clinical manifestations. Edema may be due to factors that result from vasospasm and increase the amount of perivascular fluid: increased filtration pressure, anoxia of the capillary endothelium and diminution in the flow of lymph. The increase in venous pressure in thrombophlebitis has been repeatedly demonstrated. This obviously increases the filtration pressure, which favors transudation of fluid from the vascular into the perivascular spaces. Because of the associated arteriolar spasm and evidence of diminished vascularity, there probably occurs an anoxia of the capillary endothelium that increases its permeability, permitting an excessive exudation of fluid into the perivascular spaces and thus resulting in the production of edema. Once the fluid gets out of vascular channels in such a case, it has difficulty in getting back because of the increase in the pressure on the venous side. Probably of greater significance in this condition is the fact that the pump, which is responsible for the movement of lymph, is lost. Several investigators<sup>295, 296</sup> have demonstrated that the movement of lymph is dependent on arteriolar pulsations. In the presence of marked vasospasm and increased venous pressure,<sup>261, 262</sup> arteriolar pulsations are reduced to a minimum, and the lymphatic pump is thereby lost. This decrease in lymph flow results in the stagnation of the lymph fluid and the accumulation of proteins in the perivascular fluids, thus setting up a vicious circle, in that the pressure of the perivascular fluid approaches that of the intravascular fluid, tending to prevent absorption of fluid from the perivascular spaces into vascular channels. Such a vicious circle is broken by novocain block of the sympathetic ganglia, which



causes an interruption of the vasoconstricting impulses and thus produces a re-establishment of the normal exchange of the intravascular and perivascular fluids. It has been demonstrated that blocking of the sympathetic nerves increases the flow of lymph.<sup>297, 298</sup> As a result of vasodilatation, the blood supply to the capillaries is increased, anoxia of the capillary endothelium is relieved, and excessive exudation of the vascular fluid into the perivascular spaces is prevented. By the return of the normal arteriolar pulsations, the pump, which is responsible for the movement of lymph, is re-established, and the perivascular fluid is rapidly carried away. Because of this, the edema of the extremity in a patient with phlegmasia alba dolens disappears within a relatively short time after the production of sympathetic-ganglion block. Similarly, the other manifestations associated with thrombophlebitis are relieved, probably by the increased vascularity. Pain, which is one of the most prominent manifestations of thrombophlebitis, is relieved dramatically. Prompt subsidence of fever may also be explained on the basis of a more rapid resolution of the inflammatory process by the increase of vascularity to the involved venous segment.

The results of vasodilatation obtained by novocain block have been reported in previous publications.<sup>1-4</sup> Up to the present, 71 patients have been treated by this method, with prompt relief of symptoms in all. Pain was completely and permanently relieved within fifteen minutes to half an hour after the first injection in 64 cases (90 per cent). Seven patients (10 per cent) required a second injection before the pain was permanently relieved. In 46 cases (65 per cent), the patients were fever free within forty-eight hours after the institution of therapy; in 17 (24 per cent), the temperature returned to normal within three to five days, and in 5 (7 per cent) from six to eight days. There were only 3 cases (4 per cent) in which the pyrexia lasted longer than eight days. Two of these patients had pyrexia resulting from pulmonary infarcts, one lasting twenty-one days and one thirty days, and both recovered completely. One patient had persistence of fever for ten days because of puerperal sepsis. The subsidence of edema was usually rapid. The edema completely subsided within four days or less in 40 cases (56 per cent), in from five to eight days in 23 (32 per cent), in nine to ten days in 6 (8 per cent), and in eleven to twelve days in 2 (3 per cent). Forty-four patients (62 per cent) were discharged from the hospital as cured within four to eight days after the institution of treatment. Twelve (19 per cent) left the hospital from the ninth to the twelfth day

after the institution of therapy, and 7 (10 per cent) remained in the hospital more than twelve days. All remained in the hospital longer than twelve days because of conditions other than the thrombophlebitis. The follow-up observations made on a number of these patients for periods varying from several months to over three years are particularly significant. In none has there been any evidence of recurrence of edema or of other postphlebotic manifestations. This is a particularly important fact in view of the large number of cases that developed postphlebotic edema following other forms of therapy and of the lifelong disabilities consequent to these postphlebotic manifestations.

The technic of lumbar sympathetic block has been described in detail previously,<sup>2, 3, 299, 300</sup> but in brief is as follows:

The patient is placed in the lateral recumbent position. The sites of puncture in the skin are determined by taking points approximately two and a half fingerbreadths lateral to and on a horizontal level with the spinous processes of the first four lumbar vertebrae. Twenty-gauge or 21-gauge lumbar-puncture needles approximately 9 cm. in length are employed. Each needle is inserted vertically until the transverse process of the vertebra is reached. The direction of the needle is then changed slightly to permit deeper insertion either above or below the transverse process, and the needle is inserted approximately two and a half fingerbreadths beyond the transverse process so that its point is near the anterolateral surface of the body of the vertebra where the sympathetic chain lies. Five cubic centimeters of 1 per cent procaine hydrochloride solution is injected through each needle, care being taken to determine previously that the needle is not in a vessel. It has been found that daily blocks should be performed until the temperature returns to normal and remains there. Generally, two or three blocks are sufficient.

Usually, thrombophlebitis can best be treated by conservative measures, and one need not fear the detachment of thrombi with the production of emboli, because as a result of the inflammatory reaction in the vein wall, the thrombus is firmly attached. Conservative measures are sufficient to bring about relief of symptoms and a rapid resolution of the process. Rarely, *radical intervention* is necessary. The indications for radical therapy are suppuration at the site of the thrombophlebotic process, with resultant liquefaction of the clot and the production of infected emboli. Also, in some cases of thrombophlebitis in which the infection extends proximally along the vein wall through



the perivenous lymphatics, a rapid progression of the thrombophlebitic process or a propagation of the clot occurs. In either event, division and ligation of the vessel proximal to the diseased process is imperative to prevent the extension of the process upward and possible fatal embolism and sepsis. A typical example of this is the postpuerperal sepsis in which a thrombophlebitic process involves the venous channels draining the uterus. In such cases, rapid progression of the process, together with the breaking off of infected emboli, is likely to result in a blood-stream infection and fatality. Hunter,<sup>301</sup> in 1784, was apparently the first to apply measures to combat this possibility. He states: "If the inflammation has gone so far as to make the surgeon suspect that suppuration has taken place, then the compress must be put upon that part of the vein just above the suppuration. This I once practiced, and, as I supposed, with success." Lee,<sup>302</sup> in 1865, ligated a vein above the thrombophlebitic process in 2 patients suffering from this condition. In 1880, Zaufal<sup>303</sup> successfully ligated the internal jugular vein in the treatment of pyemia originating in the internal ear. Viereck,<sup>304</sup> in 1901, showed statistically the value of vein ligation in such cases. In a collected series of 108 cases, 89 patients recovered. Apparently Freund,<sup>305</sup> in 1898, was one of the earliest surgeons to apply the method in gynecology. He performed ligation and excision of the thrombosed ovarian vein and broad ligament in 2 cases; these procedures were unsuccessful. Several years later, Bumm<sup>306-309</sup> and Trendelenburg<sup>310</sup> performed venous ligation in puerperal pyemia, the former advocating ligation by the transperitoneal route and the latter by the extraperitoneal route. Ligation or excision of the pelvic veins in the treatment of suppurative thrombophlebitis of puerperal origin has been advocated by Bumm,<sup>306-309</sup> Trendelenburg,<sup>310</sup> Sippel,<sup>311</sup> and numerous others.<sup>312-317</sup> Proximal ligation, with or without excision, has been suggested by numerous others.<sup>271, 318-328</sup> Miller,<sup>329</sup> in 1917, collected 197 cases of puerperal pyemia treated by venous ligation; 15 were approached extraperitoneally, and 182 transperitoneally. The gross mortality was 51.6 per cent. In 1921, Martens<sup>330</sup> reported 11 gynecologic cases of thrombophlebitis in which ligation of the ovarian vein, as well as that of the internal or common iliac vein, was done. In 2 cases, the vena cava was successfully ligated. Recovery followed in 7 of the 11 cases. In puerperal infections, there is considerable controversy concerning the mode of attacking vessels. Whereas gynecologists have largely preferred the transperitoneal approach, surgeons have generally preferred the extraperitoneal

approach. Martens<sup>330</sup> advocates the latter, and Krotoski<sup>331</sup> is of the opinion that the extraperitoneal approach should always be done because laparotomy produces more shock and is dangerous to these patients, who are already very ill. Moreover, there is danger that peritonitis will occur, because the ligation is not always possible in an uninvolved portion of the vein. In cases of thrombophlebitis involving the pelvic veins, it may be necessary to ligate both the internal iliac and ovarian veins. Krotoski<sup>331</sup> suggests that in an extremely ill patient it is best to ligate the internal iliac and the ovarian vein on one side through an extraperitoneal approach, but if the patient continues to have evidence of pyemia, as reflected by persistence of chills and fever, the vessels on the contralateral side should also be ligated. Otherwise, all four vessels should be ligated at the original operation. Ligation of these vessels is frequently lifesaving. If the thrombophlebitic process has extended up from the internal iliac into the common iliac vein and even into the vena cava, it may be necessary to ligate the vena cava above the thrombosed area. Krotoski states that ligation of the inferior vena cava for thrombosis has been performed in 48 cases, without any severe manifestations.

There is considerable controversy concerning the optimum time of operation. Although it is difficult to lay down definite rules, there is certainly a happy medium between the suggestion of Trendelenburg that these patients be operated on immediately after the first chill and the opinion of those who maintain that the operation should not be done until the disease has become chronic. Bondy,<sup>332</sup> Schottmüller<sup>333</sup> and Beuttner<sup>334</sup> advocate ligation of the vein after three chills and the demonstration of anaerobic streptococci in the blood culture. Whereas according to this suggestion the indications seem quite definite, we are in accord with Krotoski<sup>331</sup> that the clinical picture and sound surgical judgment are essential. A patient who looks ill, who has recurrent chills, and who apparently is losing ground should be operated on early; otherwise, a fatality is likely to occur. As early as 1912, Huggins<sup>335</sup> advised exploratory laparotomy in every suspicious case when the diagnosis is in doubt because, in his opinion, the "danger from thrombophlebitis is far more threatening than the risk of operation," if done early. If infarction has occurred, operation should be performed immediately, and procrastination in such cases is likely to mean disaster. The absence of chills in no way precludes the possibility of a septic thrombophlebitis. Krotoski reports that chills occur in only about half the cases. Schollenberg<sup>336</sup> states that, on the basis of the material

in the Zurich University women's clinic, in the cases in which a second chill was taken as an indication for operation, 67.4 per cent of patients were operated on unnecessarily, and in cases in which a third chill was taken as an indication for operation, 56.2 per cent were operated on unnecessarily. The importance of absence of chills has also been emphasized by Miller.<sup>314 329</sup>

The technic of the operative procedure and the method of approach vary according to individual operators. A distinct advantage of the transperitoneal technic is that it is possible to visualize and ligate all four of the uterine vessels through a single incision. The operation does carry a higher risk, however, because of the greater shock associated with the transperitoneal approach, and also because of the potential danger that infection of the peritoneum will occur from division of an infected vessel. It is imperative that the vessel be isolated above the point of involvement, and not only that the vessel be divided but also that a segment of vein be removed. The former is of significance, because only in this way can the propagation upward and the liberation of the emboli be prevented. The latter is necessary to obviate the extension of micro organisms through the perivascular lymphatics, which could continue if the vein is ligated only and is not divided. It is extremely desirable not only to divide the vein but also to extirpate a portion of it, since in this way the perivascular lymphatic extension can be more effectively stopped. Krotoski<sup>321</sup> emphasizes the value of careful examination of the urinary tract, because in this way it is possible to determine not only kidney involvement, but also the location of the lesion. In a case, which he reported, with involvement of the right side, there was extensive infection of the ureter and almost complete blockage on that side because of the associated inflammatory process extending from the ovarian vein. This would be a valuable procedure in determining which side should be operated on in the extra-peritoneal approach. At the time of operation, it may be desirable to drain the area of the involved vein, as has been emphasized by Krotoski. In one of our cases with suppurative thrombophlebitis of the right ovarian vein, transperitoneal exposure and resection of a portion of the vein resulted in cessation of pyemic manifestations and subsidence of fever.

Kraussold,<sup>327</sup> in 1878, successfully ligated the femoral vein in a patient who developed a suppurative thrombophlebitis following a thigh amputation. In a previously reported case,<sup>3</sup> ligation of the femoral vein, because of a suppurative thrombophlebitis in the popliteal vein, was followed by immediate disappearance of septic manifestations

Griess,<sup>328</sup> in 1913, successfully performed thrombectomy and excision of a segment of the femoral vein in a case of postpuerperal septic thrombophlebitis. Rost,<sup>329</sup> in 1916, reported 2 cases of leg amputation followed by thrombophlebitis in which ligation of the femoral vein was successful. Numerous others<sup>315 340 341</sup> subsequently reported successful proximal venous ligation in femoral thrombophlebitis and emphasized its therapeutic and prophylactic value. More recently, cases of femoral thrombophlebitis successfully operated on were reported by Pool and McGowan,<sup>323</sup> and Van Duyn and Van Duyn.<sup>342</sup>

Proximal ligation has also been employed for thrombophlebitis of the mesenteric veins, and one of the earliest cases was reported in 1907 by Brunner,<sup>343</sup> although Gerster<sup>344</sup> had previously reported 2 successful cases in which exposure and evacuation of the thrombosed vein had been done. Wilms<sup>345</sup> advocated ligation of the veins in the ileocolic angle in cases of pylephlebitis and was successful in treating a case in this manner. Braun<sup>346</sup> advised ligation of the ileocolic vein in such cases, and performed this procedure successfully in 2 patients. Melchior<sup>347</sup> was able to collect from the literature 13 cases in which the Braun procedure had been used. In 8 cases in which it was employed at the time of appendectomy, all the patients recovered. In the 5 cases in which a secondary operation was necessary, there were 4 deaths.

**Phlebothrombosis** In contradistinction to thrombophlebitis of the deep venous system, phlebotrombosis of these vessels occurs more insidiously and is frequently unassociated with marked clinical manifestations. Instead of a pyrexia, with pain in the extremity and an associated swelling and edema of the extremity, patients with phlebotrombosis have relatively little pain, usually little or no fever and generally no swelling. Of greater diagnostic importance is the increasing pulse rate—the "stepladder pulse" first emphasized by Mahler.<sup>348</sup> When pain is complained of, it is usually in the calf or in the sole of the foot, because, as Neumann<sup>349</sup> has shown, the thromboses are generally limited to the veins of the calf or foot. He found that the foot veins were involved in 71 per cent, the leg veins in 87 per cent, and the thigh veins in 22 per cent. Solitary thrombosis occurred in the calf veins more frequently than in other veins. Solitary calf-vein thrombosis occurred in 29 per cent, solitary plantar-vein thrombosis in 12 per cent, and both calf-vein and leg-vein thrombosis in 57 per cent. Rossle<sup>61</sup> in post-mortem studies found that 25 per cent of all cases had calf-vein thromboses. Of greater importance than spontaneous pain is that elicited by pressure

on the plantar aspect of the foot, on the medial aspect of the foot just beneath the medial malleolus or in the calf, or by forced dorsiflexion of the foot in the popliteal region, the so-called "dorsiflexion sign of Homans." On the basis of extensive anatomic studies, Bragard<sup>350</sup> found that examination of the lower end of the femoral vein was best performed by having the patient sit with his legs separated and externally rotated. This causes the hamstring muscles to be rolled to the inner side, bringing the femoral vein into a more superficial position. The examiner sitting in front of the patient can palpate with both hands the two femoral veins in their lower portions and can determine better whether there is tenderness and induration. For examination of the calf veins, he advocated grasping the muscles of the calf behind the tibia and eliciting tenderness by firm pressure. Whereas these patients do not appear to be so ill as those with thrombophlebitis, the possibility of serious trouble is much greater; because of the lack of the inflammatory reaction in the vein wall, the thrombus is either only loosely or not at all attached to the vein wall, and the chance of its becoming detached, with resultant infarction or massive embolism, is considerable.

As in phlebothrombosis of the superficial veins, *conservative therapy* is indicated in the absence of rapid progression and evidence of infarction. The application of elastic bandages to the involved extremity, extending from the metatarsal phalangeal joints up to the groin, is desirable. The thigh should be flexed and elevated to an angle of 45°, and the leg and foot should be elevated above the level of the knee. Passive and slightly active motion of the foot at the ankle is encouraged. After twenty-four to forty-eight hours, the motion can be made against resistance. This favors the movement of the blood in the deep veins. The application of a heat tent over the lower extremities is of great value, not only because of the support it offers to the bedclothes, but also because of the vasodilatating effect of the heat.

Hirudinization and heparinization have been employed and may be of value in these cases of deep-vein phlebothrombosis. Whereas heparinization has been advocated prophylactically and therapeutically, it seems to us that its value depends on the prevention of propagation of thrombi and the production of emboli. For such purposes, it appears that proximal ligation is a much safer and more reliable procedure.

Vasodilatation, by means of vasodilatory drugs such as papaverine, anaphoresis with Mecholyl or the use of sympathetic block is of value in cases of phlebothrombosis as well as in those of thrombophlebitis. The results obtained are not so dramatic as those in thrombophlebitis because such

patients do not have the marked pain, swelling and fever that patients have with thrombophlebitis.

Whereas the manifestations in phlebothrombosis of the deep veins may subside completely under conservative therapy, because the thrombus is loosely attached, it is frequently necessary to resort to *radical therapy*. This is indicated in those cases in which there is rapid progression of the thrombotic process, as evidenced by upward extension of tenderness, a persistent elevation of pulse rate, and fever. The development of an infarct is an extremely important indication for radical therapy. Zink<sup>351</sup> states that in 70 per cent of cases with fatal pulmonary embolism there was a hemorrhagic infarct, indicating a previous embolism. Bahls<sup>357</sup> emphasizes the importance of restlessness, together with an elevation of the pulse, in a patient who is otherwise doing well. The patient senses that something is wrong. Bahls believes that these are premonitory manifestations of a fatal pulmonary embolus. Other indications for radical therapy, as emphasized by Homans,<sup>168</sup> are the failure of the subsidence of symptoms under conservative therapy and the return of manifestations after the patient is allowed up and after the symptoms have originally subsided. Sears<sup>326, 327</sup> believes that all patients with thrombosis of the calf veins should have proximal-vein ligation as soon as the diagnosis is made. Thrombectomy has been advocated by Låwen<sup>273</sup> and Kulenkampf,<sup>352</sup> the former extracting the thrombus through an opening in the femoral vein, the latter through the saphenous opening. Both attempt to save the deep venous system by suture of the vein wall. Lange<sup>353</sup> also advocates thrombectomy, but Fründ<sup>354</sup> states that ligation should also be done. Leriche and Geisendorf<sup>355</sup> performed thrombectomy but also resected a segment of the femoral vein. Whereas, theoretically, thrombectomy and suture of the vein seem desirable and although the experimental work of Hintze and Zollenkopf<sup>356</sup> appears to support the contention that these veins again function, we believe not only that it is unnecessary to attempt to save the vein but that it is actually dangerous. In one of our cases with extensive phlebothrombosis of the deep venous system and pulmonary infarction, the common iliac vein was ligated at its junction with the vena cava, and a concomitant resection of the third and fourth sympathetic ganglia performed. The patient recovered rapidly and has remained free of all previous manifestations. Homans<sup>168</sup> suggests saving the vein and heparinizing the patient. In one of his cases in which this was done, embolism recurred, thus making it necessary to divide the common iliac vein, following which embolism ceased and the leg became functionally useful. This case, it seems



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## THE MANAGEMENT OF GONORRHEA\*

## VI. The Sulfonamides

## Neisserian Medical Society of Massachusetts

## SULFANILAMIDE

**S**ULFANILAMIDE should not be used in the treatment of gonococcal infections. Early reports of its high efficiency were commonly in error because of failure to evaluate cure by cultural methods. The immediate clinical response was good in a large number of cases, but subsequent clinical relapse was common, and cultural studies made by many later observers disclosed that innumerable asymptomatic carriers were being produced. These carriers remain potential spreaders of infection for many months.

## SULFAPYRIDINE

Sulfapyridine cures a much higher proportion of cases, but it causes more serious reactions than sulfanilamide does. Since a newer drug, sulfathiazole, is equally effective and causes few immediate reactions, this should be, at present, the drug of choice.

## SULFATHIAZOLE

There is much excellent evidence, based on careful and extensive cultural study, that sulfathiazole cures as high a proportion of gonococcal infections, in either sex, as any other sulfonamide now available. Of the failures, some do not respond at all, and the remainder either relapse or become asymptomatic carriers for variable periods.

Although many excellent treatment schemes have been and are still used, the following dose has the advantage of being simple and rapidly effective: 2 gm. daily for ten days; the daily dosage is usually divided into four doses of 0.5 gm. every four hours. The dose for children is 30 mg. per pound of body weight, but the total daily dose should not exceed 2 gm. The fluid intake should not be restricted.

In men, if there has been no clinical improvement by the fifth day, the drug should be discontinued for the time being, for its continued

use will accomplish no favorable result. The clinical picture in women is so often confused by other conditions, however, that it is the rule to give the full course in every case and to depend on bacteriologic study for proof of response.

Infections that fail to respond to one course of sulfathiazole may often be cured by a second course, similar to the first, following a rest period of a week or ten days. More than two consecutive courses of the drug, however, are of questionable value.

In definite drug failures, careful search should be made for the possible cause of failure, and recourse should be had to local treatment. In some cases, fever therapy may be indicated.

The patient should be kept under observation during the course of sulfathiazole therapy because reactions may occur as a result of the administration of any of the sulfonamides. If there is persistent vomiting, rash or other severe reaction, the drug should be discontinued. Moderate nausea will be reported by an occasional patient, but is not ordinarily a cause for stopping the drug. There is no need for determining blood levels when the recommended dose is used, for concentration of the drug in the blood seems to have no relation to the clinical or bacteriologic result. Blood counts and hemoglobin determinations may be indicated for some patients.

## DETERMINATION OF CURE

When treatment has been concluded, the patient should be directed to abstain from unprotected sexual contacts for at least three months. Relapse should ordinarily occur within this period, if it is to occur. If cultural facilities are available, cultures of prostatic secretion and urine sediments in men and of exudates from the cervix and the paraurethral (Skene's) glands in women should be made from four to six times during this period. Smears, also, should be examined, but negative smears should not be relied on as evidence of cure. More than 3 to 5 pus cells per oil-immersion field in prostatic secretions are significant of prostatic infection of some kind (not necessarily gonococcal), but freedom of prostatic secretion from pus is not evidence of cure of a gonococcal infection.

In some women who have gonorrhea, the vaginal discharge continues or reappears after treatment

\*In 1934, the Neisserian Medical Society of Massachusetts undertook the publication, in the *New England Journal of Medicine*, of a series of papers on the management of gonorrhea.<sup>1-5</sup> Shortly after the appearance of the fifth paper, in 1937, the sulfonamides were added to the therapeutic armamentarium. Until now, the Society has not been satisfied that enough data were available concerning the performance of these new drugs to permit sound conclusions about their worth. This sixth paper in the interrupted series is now presented as an expression of the Society's opinion concerning the place that the better of the sulfonamides should have in the therapy of gonococcal infection.

Since the American Neisserian Medical Society was about to issue a somewhat similar statement based on its wider experience, the two statements were combined, and will appear in essentially identical language. That of the American Neisserian Medical Society will appear in the *Transactions* for 1941.

has been stopped. It is worth while to search for other causes in these cases before concluding that the gonococcal infection has not been cured, or that the patient has been reinfected.

#### SOME VALUABLE ADVANTAGES TO BE GAINED

It is of the greatest advantage to begin treatment of infections in women immediately, without waiting for laboratory confirmation of the diagnosis, if the history of exposure or a known infection in the sexual partner, in addition to clinical evidence in the patient, points to gonococcal infection. Prompt treatment usually prevents extension of the infection into the pelvic cavity, or controls it if it has already occurred. The risk of permitting an infection to spread upward is much greater than the risk of using the drug in a case that may not be a gonococcal infection. Smears and, if possible, cultures, should be made at the first visit in every case, however, since they may help to establish the diagnosis. Once treatment is begun, they are likely to be negative.

### CLINICAL NOTE

#### THE CONTROL OF POSTOPERATIVE TONSILLAR HEMORRHAGE\*

JOHN R. NOYES, M.D.†

BROCKTON, MASSACHUSETTS

**B**LEEDING following tonsillectomy usually occurs either within twelve hours following operation or between the fourth and sixth postoperative days. When it occurs during the latter period, it is usually the result of a slough due to imperfect healing. The bleeding is apt to be of the slow capillary type but is inclined to be persistent, and it is often difficult to find any distinct vessel from which it is coming.

Since general surgical principles have been applied and ligatures liberally used at the time of operation, the incidence of hemorrhage has been greatly reduced, but the condition still occurs frequently enough to keep the surgeon constantly on the alert, and anything that will make this troublesome problem easier should be welcomed.

Many methods, both mechanical and chemical, have been used in the past, but none has seemed quite ideal. The following procedure for controlling such hemorrhages was developed entirely by accident.

In the summer of 1920, I performed a tonsillectomy on an 18 year-old girl. Five days later, I was

Since sulfathiazole seems to cure a high proportion of gonococcal infections in both sexes, the prompt use of this drug should result in an early "chemical quarantine" of many of the infections. Every effort should be made, however, to keep the patient under sexual control for at least three months after apparent cure.

There is reason to be optimistic over the eventual control of gonorrhea, for it should now be possible to cure the disease much faster than it can spread. The medical profession has at hand a medium through which, if properly used, one more dangerous and prevalent communicable disease may be added to those that were once serious public health problems.

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called to her home on account of bleeding from the throat. Examination showed that it was coming from the left tonsil wound, from what appeared to be a piece of tonsillar tissue.

Novocain was injected around the supposed piece of tonsil so that it could be removed, because it is well known that the removal of such tabs will sometimes stop bleeding. Immediately after the injection, the bleeding ceased. Further examination showed the supposed tonsillar tab to be only an organized clot.

This experience was impressive, and it led to the adoption of the same method in every case of delayed hemorrhage that I have treated within the last twenty years, a total of 126 cases.

Bleeding was promptly and permanently checked in every case except one. The patient in this case was a forty three year-old woman with a systolic blood pressure of 260. Hemorrhage occurred six hours after operation. It was necessary to place a ligature around the bleeding point.

The first step in this method is to gain the cooperation of the patient; this is time well spent. Next, the clot that is always present at the site of bleeding is swept out with a piece of gauze on a curved hemostat. The bleeding point is found if possible, and 1 or 2 cc. of a 1 per cent novocain solution containing 0.06 cc. (1 minim.) of 1:1000 adrenalin solution per cubic centimeter is injected *superficially* around it. If the bleeding point cannot be found, the solution is injected at various places in the wound until bleeding stops.

\*Read before the New England Oto-Laryngological Society.

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Ten cubic centimeters can safely be used. A syringe, similar in type to the small one commonly used by dentists, holding a 5-cc. ampule of sterilized solution, is used. The same syringe is used for tonsillectomies under local anesthesia. This method can be employed with a minimum of discomfort to the patient, and can easily be applied without anesthesia in quite young children.

The control of the bleeding is effected by the mechanical pressure produced by the solution, together with the vasoconstrictor action of the adrenalin.

The danger of infecting the deep tissues of the neck when injecting through a septic field has always been kept in mind, but no infection has occurred. In only a few cases have I painted the area to be injected with an antiseptic solution.

This method has been recommended to several associates, and all who are using it report uniformly good results. Its chief value lies in its simplicity and effectiveness. I am now using it to control bleeding at the time of the removal of tonsils, and also for spontaneous nasal hemorrhages.

47 West Elm Street

## MEDICAL PROGRESS

### ARTIFICIAL FEEDING OF INFANTS\*

R. CANNON ELEY, M.D.†

BOSTON

THE present method of artificial infant feeding has become as simplified as the earlier percentage methods were complicated. Yet, in spite of this advantage, one is frequently surprised at some of the types of feeding that are encountered both in private practice and in public clinics. A consideration of the nutritional needs of the normal infant, the method of determining the formula, the expected vitamin requirements and the age periods at which food substances other than milk are added to the diet is therefore presented.

In determining the nutritional requirements of a normal infant, one must consider not only the structural requirements—that is, protein, fat, carbohydrate minerals and water—but also the energy requirements for basal metabolism, exercise, growth and repair, and loss through stools (a total of approximately 40 calories per pound).

The protein requirements of the normal infant are satisfied by a daily minimum of 1.5 gm. per pound of body weight, although on rare occasions it may be preferable to increase this amount to 2 gm. Cow's milk conveniently contains this amount of protein in 1½ ounces of milk, so that it becomes quite simple to multiply the weight of the infant by one and a half and thus derive the number of ounces of cow's milk required to meet the protein needs of the baby. This minimum requirement of cow's-milk protein is somewhat greater than that of human-milk protein, since cow's milk is relatively deficient in certain amino acids.

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Although fat and carbohydrate furnish a certain amount of the structural requirements, they are primarily employed as available sources of energy. The percentages of fat (3.5 to 4.0) present in both mother's and cow's milk are approximately the same, and in the healthy infant can usually be tolerated without difficulty. In fact, when an infant is artificially fed, the percentage of fat in the formula is less than 3.5 to 4.0, owing to the dilution of the whole milk by the addition of water. Carbohydrate, which in the artificially fed infant should afford approximately one third the total number of calories, may be in any clean and inexpensive form such as cane sugar, Karo corn syrup and Dextri-Maltose. Although the sugar present in human milk is lactose, and although many are of the opinion that lactose is unquestionably the sugar of choice for these infants, it has been more than difficult to demonstrate any appreciable difference between infants receiving this sugar and those receiving a less expensive form, such as corn syrup.

The total fluid requirement for the normal infant varies, according to the age and weight of the baby. In the early months of life, and particularly during the first few days of life, this need can be satisfied by 2½ to 3 ounces per pound of body weight daily. As one might expect, this requirement is subject to change, such as in hot weather and in the presence of diarrhea, when large amounts of fluid are being lost. The mineral and salt content of cow's milk, although much greater than that of mother's milk, is usually tolerated very well by the infant and, except in the presence of pathologic conditions, adequately supplies the need.

When one considers the vitamin content of milk, exclusive of irradiated milk or milk ob-

tained from a herd receiving irradiated yeast, vitamins A and B are usually adequate, but C and D are present in such small amounts that for practical purposes they must be considered inadequate. The average daily requirements of these substances can be met by the addition to the diet of  $1\frac{1}{2}$

TABLE 1. Commonly Employed Sources of Vitamins

SUBSTANCE	VITAMIN			
	A int units	B <sub>1</sub> int units	C mg	D int units
Human milk (quart)	2000	200	50	100-200
Cow's milk, pasteurized (quart)	2000	150	0-4	20
Cow's milk, evaporated (quart)	4000	300	None	40
Orange juice (ounce)	40	20	10-15	None
Cod liver oil, U.S.P. (2 teaspoonfuls)	4800	None	None	630
Oilum percomorphum (5 drops)	6500	None	None	925
Vitosterol (5 drops)	None	None	None	1000
Halibut liver oil (10 drops)	8500	None	None	145
Halibut liver oil with vitosterol (5 drops)	4250	None	None	650
Brewer's yeast (10 grams)	None	126*	None	None

\*Also vitamin G (B<sub>2</sub>), 160 Sherman units

ounces of orange juice or 3 ounces of tomato juice (25 mg. or 500 international units of vitamin C) and 2 teaspoonfuls of cod-liver oil (400 international units of vitamin D). Table 1 presents the more commonly employed sources of these vitamins.

Since the energy requirements of a normal infant have already been mentioned, a second table

TABLE 2 Average Energy Values and Measures of Food Substances in the Infant's Formula.

FOOD SUBSTANCE	ENERGY VALUE cal /oz	MEASURE teaspoonfuls/oz
Mother's milk	20	2
Cow's milk (4 per cent fat)	20	2
Home skimmed milk	13	2
Fat free milk	10	2
Cane sugar and Karo corn syrup	120	2
Lactose	120	3
Decalin Maltose	120	4
Starch and uncooked cereal	100	3
Cod liver oil	270	2
Orange juice	15	2

(Table 2) presents the caloric values of the various substances that constitute the diet of the young infant.

Attention should also be directed to the method employed in determining the actual amounts of milk, carbohydrate and water that constitute the formula. The daily caloric need is first obtained by multiplying the weight of the baby by a standard number of calories. In general, 45 to 50 calories per pound are adequate during the first months of life, whereas 40 to 45 calories are essential during the second half of the first year. As previously stated, the protein requirements are usually satisfied by  $1\frac{1}{2}$  ounces of cow's milk per pound of body weight, so that if one assumes that the baby weighs 8 pounds, one would need 12 ounces of cow's milk. This would not only contain the needed protein and minerals but would

also furnish 240 of the necessary 360 calories, leaving the balance of 120 to be supplied by added carbohydrate. (It is advisable that approximately two thirds of the total caloric requirement be supplied by the milk and only one third by carbohydrate.) The total fluid volume is obtained by adding a quantity of water so that the resulting amount is approximately  $2\frac{1}{2}$  ounces per pound of body weight. To obtain this, one would add about 7 ounces of water, and the formula would then be:

Whole milk	12 oz (240 calories)
Carbohydrate	1 oz. (120 calories)
Water	q. s. ad 20 oz. ( 0 calories)
	20 oz. (360 calories)

As the infant gains in weight, it becomes necessary to alter the formula to meet the increased demands. For example, when the baby reaches 12 pounds the formula would be:

Whole milk	18 oz (360 calories)
Carbohydrate	$1\frac{1}{2}$ oz. (180 calories)
Water	q. s. ad 30 oz. ( 0 calories)
	30 oz (540 calories)

The formula is prepared in the following manner:

Dissolve the specified amount of carbohydrate in the water, and add the solution to the milk. Boil this mixture over direct heat for three minutes, stirring constantly. When the mixture has cooled, pour it into a sterile graduate, preferably glass, or some measuring container, and add to this a sufficient quantity of sterile water to make the final volume. Divide the formula into the desired number of feedings by pouring the necessary amount into sterile bottles, which are then capped with sterile rubber stoppers. As soon as the bottles have cooled, they may be placed in the ice chest until needed. The number of feedings, or bottles, given to the baby each day depends not only on the age and weight but also somewhat on the infant itself, for it is certainly true that some babies gain and do well on a small number of daily feedings. However, the baby usually requires one feeding every four hours during the first few weeks of life, after which five daily feedings are ample.

Formulas prepared from evaporated or dried milk have found a useful position in infant feeding, and certainly there are occasions, as well as circumstances, when they can be employed to advantage. The chief objection to the use of these proprietary forms of milk is that it frequently becomes necessary to alter the protein or especially the fat content of the infant's formula (such as in the presence of an infection), and if such forms of milk are being employed this alteration

becomes practically impossible. Another objection is that there are no legal standards for the grade of milk used in these preparations. It is a common impression that evaporated milk produced by a given manufacturer is always the same, but this is not necessarily true: if the company is producing its product in several sections of the country, the grade of the milk varies according to the grade of the milk of the locality. In spite of these differences, experience has shown that evaporated milk may be employed as a satisfactory source of food for infants. When using it in preparing a formula, one has only to remember that half the water has been removed from the milk in its preparation, and that when this is replaced each ounce of the mixture is equivalent to an ounce of cow's milk. For example, if evaporated milk were used in the previous formula, the amounts would be: evaporated milk, 9 ounces; carbohydrate,  $1\frac{1}{2}$  ounces; and water, sufficient to make 30 ounces.

This simple mathematical determination of an infant's food requirements would make infant feeding a simple procedure if the resulting equation could be applied to all babies. Unfortunately, however, this cannot be done, since the requirements for each baby vary over a wide range, depending on the infant's ability to utilize the food, his activity and so forth. For example, one baby may gain and do well on 35 calories per pound, whereas another baby of the same age may require 50 calories per pound. Since it is impossible to know this beforehand, and since babies on a high-calorie intake are apter to develop digestive disturbances than those on a low-calorie intake, it is always safer, and therefore advisable, to start an unknown infant on a low-calorie intake and then to increase the diet should it prove inadequate. Again, an undernourished infant usually needs a larger amount of food per pound of body weight than a relatively normal baby, and as a rule the requirements more nearly approximate those based on the expected weight rather than those based on the actual weight.

Failure of a baby to gain on a well-balanced formula does not necessarily imply that the formula per se is at fault, and it certainly should not be considered an indication to change to something else—as it too frequently is. Any change in the formula should not be undertaken until after a thorough physical examination of the baby has been made and all evidence of infection—acute, chronic, enteral or parenteral—has been excluded. The formula is rarely guilty.

In those cases in which the infant has been breast-fed, if even for only a few days, little difficulty will be encountered when a formula feeding is substituted for a breast feeding. If necessary,

one can replace one breast feeding by one formula feeding each day until the baby is weaned. On occasion, the mother may be unable to nurse her baby, and it becomes necessary to feed the infant artificially from the very beginning. In such cases, it is advisable to prepare a weaker formula, that is, one that contains less than 20 calories per ounce, since the digestive system of the newborn infant may not be able to tolerate a stronger mixture. An adequate formula for this purpose is one containing equal parts of milk and water and less carbohydrate than usual: for example, whole milk, 10 ounces; carbohydrate,  $\frac{1}{2}$  ounce; and water, sufficient to make 20 ounces. This formula may be offered two or three times on the second day of life, four times on the third day, and every four hours thereafter. Once this type of feeding has been satisfactorily established, the strength of the formula may be gradually increased until each ounce contains 20 calories.

I have already mentioned the addition of vitamins to the dietary and now need to consider only the periods at which other foodstuffs may be introduced. Although there may be rare cases in which it is necessary to add other foods to the diet, most infants do not require these substances before the fifth month of life. At this time, cereal may be added at the 10-a.m. and 6-p.m. feedings, being served with some of the formula poured over it. As soon as this is accepted by the baby, a small amount of stewed fruit, usually in the form of applesauce, may be included at 6 p.m. Strained vegetables, egg yolk and beef juice are frequently given by the sixth or seventh month. With the addition of these foods, one should gradually reduce the added carbohydrate in the formula, since these calories are available through the additional food. Experience has shown that it is not advisable to remove all the sugar at once but to reduce it every few days until it has been entirely removed. By such a process, one is often able to omit the formula and have the baby on three daily feedings by the ninth or tenth month of life.

I have deliberately omitted the quantities of each food substance that the baby should take. The baby is a very good judge himself, and if one only begins with reasonably small amounts and increases them as the baby shows his inclination and desire for more, one will go far in having not only a happy baby but also a happy mother. To say that the baby *must* take one tablespoonful of one substance and two of another at a specified feeding is as absurd as insisting that each baby *must* have a quart of milk a day. Insistence on such impractical principles as these usually results in an unhappy and stubborn infant who soon rebels against all his food.

# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

## CASE 27321\*

### PRESENTATION OF CASE

An eight and-a-half-year-old girl was brought to the Outpatient Department with a complaint of vomiting. Her past history was not remarkable except for an appendectomy five years previously, and occasional attacks of abdominal pain and vomiting since that time. A mild upper respiratory infection had been present for the previous week.

While on a trip with her family two days before admission, the child had a strawberry milk shake and fried clams, other members of the family had the same type of food at that time. About half an hour later, she began to complain of low abdominal pain, and she vomited once. That night, she vomited three times but did not appear to be very sick. On the following morning, the mother gave her an enema, with a moderate fecal return. This was followed with another shortly thereafter, without results. During that morning, she ate nothing and vomited three times. The family physician was consulted, and advised an additional enema, which was unproductive, and a mild laxative, which was immediately vomited. The child had no fever, and played normally the rest of the day. On the day of admission, the abdominal pain seemed very much diminished, but she vomited several times. She passed no feces or gas by rectum. The family physician was called again that morning. After a flat plate of the abdomen was taken, which showed dilated loops of bowel, he advised that the child enter the hospital.

Examination revealed general dehydration, with sunken eyes, slight cyanosis of the lips and rapid, shallow respirations. The abdomen was distended and tympanic, with moderately active peristalsis. There was no spasm or tenderness by abdominal or rectal palpation.

The temperature was 102°F, the pulse 120, and the white cell count 15,000.

Within a few minutes after admission, a marked change in the patient's condition became apparent. The pulse became imperceptible, and cyano-

sis became more marked. Twice, she vomited large amounts of thin, brownish fluid material, which on later examination proved to be guaiac positive. There was no fecal odor to this material. During the next few minutes, her extremities became cold and pulseless, her breathing became more rapid and shallow, and she became disorientated. Restlessness became more marked, and the patient became comatose. Respiration and heart beat stopped apparently at the same time. There was no response to the intracardiac administration of adrenalin. Artificial respiration was attempted without success. Exitus occurred approximately twenty minutes after arrival at the Outpatient Department.

### DIFFERENTIAL DIAGNOSIS

DR ROBERT R. LINTON: There are certain things in the past history of this patient that are of interest and bear a definite relation to the outcome. The fact that she had an appendectomy five years before admission should be noted, and also the fact that she had abdominal pain and vomiting on occasions after the appendectomy. I do not believe her mild upper respiratory infection had anything to do with her exitus. Nor do I believe the strawberry milk shake and fried clams eaten prior to the onset of the terminal illness had any bearing on her condition, since she vomited within half an hour after taking them. It is possible that the taking of food, and I think it could have been any kind of food, might have precipitated her trouble. The most important thing to me is the fact that she had complete obstruction shortly after the onset of her illness. She had a number of enemas which were unproductive. She had a mild laxative, which was vomited, so that we do not know whether it would have produced results or not—probably not. Her local doctor showed wisdom in having a flat abdominal x-ray plate taken; this is a useful diagnostic procedure in abdominal conditions, especially when one may be dealing with intestinal obstruction. It is reported that the plate showed dilated loops of bowel. I am sorry we cannot see that plate to determine whether the dilated loops were small bowel or large bowel, since such a differentiation is of considerable importance in making a decision of what the trouble is.

The patient was admitted to the hospital, and according to the physical examination, she was extremely sick. The cyanosis of her lips, I think, is a very important point. Her temperature was 102°F, and she had a pulse of 120. The abdomen on examination showed distention, which would go with the x-ray report of dilated intestinal

\*This case is presented through the courtesy of the Children's Hospital Boston.

loops. I am a little surprised that she had moderately active peristalsis. I should almost think she was too sick for active peristalsis to have been present. At least, peristalsis rules out the possibility that she had peritonitis, since active peristalsis in the presence of peritonitis does not occur. She had no spasm or tenderness by abdominal or rectal examination. That also helps one in ruling out peritonitis, although I have seen cases of generalized peritonitis in which there was no spasm and practically no tenderness. The white-cell count was 15,000, which is consistent with either peritonitis or intestinal obstruction.

The extraordinary thing about this patient is that she died so shortly after admission to the hospital. Because she was vomiting large amounts of fluid, one wonders a little whether she died from suffocation following the aspiration of vomitus, but the story we have is not of this nature. The history describes the vomitus as thin, brownish fluid, a description which is typical — except for the fact that there is no mention of a fecal odor — of intestinal obstruction and probably small-bowel obstruction. It is possible that she was in such dire straits from dehydration and electrolyte loss that she could succumb as quickly as this. I have seen such deaths occur. I remember seeing a man in the Emergency Ward who was admitted in a condition very similar to that of this patient; he succumbed while being sent from the Emergency Ward to the operating room, so that people can die quickly of intestinal obstruction. The fact that the brownish fluid was guaiac positive is further evidence of intestinal obstruction. Such fluids are usually guaiac positive, owing to small capillary hemorrhages and stasis within the vascular system of the bowel.

My belief is that this patient died of acute intestinal obstruction, which resulted from the fact that a loop of ileum had become adherent to the appendectomy scar in the right lower quadrant.

A PHYSICIAN: Could she have had a pancreatitis?

DR. LINTON: I have never seen pancreatitis in such a young person.

DR. MILTON J. QUINN: Could she have had a condition associated with a Meckel's diverticulum?

DR. LINTON: If she had had, the diverticulum might have perforated, thus causing a peritonitis. It is possible, of course, to have intestinal obstruction or intussusception from a Meckel's diverticulum. I suppose I am assuming a little too much in thinking that the surgeon who operated on her five years previously ruled that out. It is possible that he did not, and there might have been a Meckel's diverticulum. It is a distinct

possibility and should have been included in the differential diagnosis.

#### CLINICAL DIAGNOSIS

Intestinal obstruction, acute.

#### DR. LINTON'S DIAGNOSIS

Intestinal obstruction due to postoperative adhesions.

#### ANATOMICAL DIAGNOSES

Intestinal obstruction, acute, complete.

Volvulus of terminal ileum.

Old adhesions between ileum and abdominal wall at site of old appendectomy incision.

Pulmonary edema, severe, acute.

Bacteremia (unidentified, anaerobic, spore-bearing, gram-positive bacillus), agonal.

#### PATHOLOGICAL DISCUSSION

DR. SIDNEY FARBER:\* Dr. Linton's first suggestion was the finding that we made at post-mortem examination. A volvulus of the small intestine passed around old adhesions, which connected the ileum to the abdominal wall at the site of the old appendectomy incision. The small bowel above the point of obstruction was very much distended. The walls of the small bowel were edematous. In its lumen, there was found about 500 cc. of rather thin dirty fluid, which had a fecal odor. On microscopic examination, the discolored portion of ileum was not necrotic in all places: there were areas where the mucosa was intact. The impression given by gross and microscopic examination was that the obstruction had been an intermittent affair.

The spleen was about half the normal size. Throughout the body, there was evidence of rather widespread vascular collapse. The veins all through the abdominal cavity were greatly distended with blood. The lungs were the site of marked edema.

The brain was approximately of normal weight and showed externally only moderate edema. On section after the brain was fixed, however, there were a number of small areas of destruction scattered throughout the brain, giving a Swiss-cheese appearance. These areas could be correlated with the presence in the lung on culture and in various organs in the body on section of gram-positive, spore-bearing bacilli, which looked like *Clostridium welchii* but which did not behave like this organism on guinea-pig protection studies. The organisms must have reached the blood stream just before death. There was no cellular reaction to these bacteria anywhere in the body.

\*Assistant professor of pathology, Harvard Medical School; pathologist, Children's Hospital.

In summary, the postmortem showed acute intestinal obstruction caused by volvulus brought about by old adhesions between the ileum and the abdominal wall at the site of the old appendectomy wound.

DR. LINTON: It seems to me that too many cases of this nature are occurring. We have had a number, and I have seen one very recently. It is a condition that can be prevented, and it merely means a careful toilet when a surgeon is closing the peritoneum. In an adult, there is practically always sufficient omentum to interpose between the loops of the small bowel and abdominal wound. In a child, the omentum is not so large, and one cannot always do it so readily. For that reason, one should take more care and be sure that the wound presents an absolutely smooth surface from within the peritoneal cavity, so that the small bowel cannot become adherent to it. We have had within a year a patient very similar to this in whom the loop of ileum had become adherent to the stump of the appendix, which had not been infolded or invaginated into the cecal wall. That patient, even though he did not die so quickly as this one, did succumb while in the hospital and while an effort was being made to prepare him for operation. He drained an unusual amount of fluid from the Miller-Abbott tube, and it was never possible to hydrate him. It seems too bad that patients should lose their lives from something that can be prevented very easily if a careful surgical technic is used.

DR. HAROLD L. HIGGINS: It impresses me that these cases often carry on with minimal symptoms for two or three days after the initial vomiting. This child apparently was not sick enough for the attending physician to spot the fact that it was a case of intestinal obstruction. In one case that I saw recently, the doctor who cared for it got the impression it was merely so-called "intestinal flu."

DR. TRACY B. MALLORY: You were inclined, Dr. Farber, to assume that the obstruction at the start was intermittent and became permanent only shortly before exitus?

DR. FARBER: Yes.

## CASE 27322

### PRESENTATION OF CASE

*First Admission.* A forty-eight-year-old housewife entered the hospital complaining of frequent colds, sinusitis, easy fatigability and a chronic cough with small amounts of green sputum. She had also noticed a gain in weight.

Physical examination showed infected tonsils;

the blood pressure was 125 systolic, 80 diastolic. A tonsillectomy was performed, and the patient discharged one week later.

*Second Admission* (ten months later). The patient was admitted primarily for back strain following a fall a few days previously. In addition to chronic sinusitis, which still troubled her, she complained of occasional nausea and vomiting in the morning during spells of coughing and, in addition, a feeling of lethargy, sleepiness and anorexia.

In the previous five years, her periods had become irregular and scanty, and these symptoms were accompanied by hot flashes and an increasing nervousness. There had been a weight gain of 25 pounds in the previous two years, although presumably she had followed a 1200-calorie diet. For twenty-three years, the patient had been in the habit of drinking at least two cocktails before dinner each night. At no time had jaundice or tarry stools been noticed.

On examination, the patient was moderately obese and in no distress. The heart was normal, and fine rales were heard at the lung bases; the blood pressure was 150 systolic, 110 diastolic, the pulse 90 to 100. The liver was palpable four fingerbreadths below the costal margin, and a little tenderness was elicited on deep palpation. Slight tenderness was present over the lumbar spine and sacrum.

The urine showed a + test for albumin. The blood showed a red-cell count of 4,120,000 with a hemoglobin of 14.8 gm. (photoelectric-cell technic), and a white-cell count of 7100 with 52 per cent polymorphonuclears, 29 per cent lymphocytes and 19 per cent mononuclears. The sedimentation rate was 50 mm. in one hour; the nonprotein nitrogen was 17 mg. per 100 cc., the protein 7.0 gm., and the serum van den Bergh 2.2 mg., biphasic. A follicle-stimulating-hormone test was positive; the basal metabolic rate was +35 per cent; and a blood Hinton reaction was negative.

The patient was on a low-calorie diet, and two days after admission acetone was noticed on her breath. The urine then showed a +++ test for acetone and + test for bile; the blood sugar was 88 mg. per 100 cc. The diet was readjusted, and two days later both the acetone and bile had disappeared from the urine.

The patient was discharged on the fifth hospital day, with diagnoses of obesity, menopause, chronic bronchitis and sinusitis. Treatment consisted of a low-caloric, high-vitamin diet and endocrine preparations.

*Final Admission* (fifteen months later). In the interval between admissions, the patient had suffered from essentially the same symptoms as be-



fore — nervousness, lethargy and occasional nausea and vomiting. She was somewhat apprehensive, and her pulse ran between 110 and 120.

One week before admission, the patient suddenly developed a digestive upset, with malaise, nausea and vomiting, diarrhea and, finally, prostration. Her physician noticed that she was jaundiced and advised hospitalization.

The family and past histories were irrelevant.

On examination, the patient was listless and apathetic, but rational. Her skin was dry, hot, dehydrated and markedly jaundiced, with a mild telangiectasia of the hands and face. The heart was normal; moist rales were heard throughout the dependent parts of the left lung; the blood pressure was 90 systolic, 60 diastolic. The abdomen was distended, tense and tympanitic, with shifting dullness but normal peristalsis. Liver dullness reached the fifth interspace, and the organ could be felt on a level with the iliac crest in the mid-clavicular line.

The temperature was 97°F., the pulse 110, and the respirations 22.

The urine showed a ++ test for albumin, with a yellow sugar reaction and a ++ test for bile. The bile-stained sediment contained many hyaline and finely granular casts, a rare cellular cast and 50 white blood cells per high-power field. The blood showed a red-cell count of 1,590,000 with a hemoglobin of 65 per cent, and a white-cell count of 18,400 with 76 per cent polymorphonuclears. The nonprotein nitrogen of the blood serum was 15 mg. per 100 cc., the icteric index 50, a van den Bergh 10.9 mg. per 100 cc.; a brom-sulfalein test showed 100 per cent retention of the dye in the serum. The total serum protein was 6.9 gm. per 100 cc., the albumin being 3.5 gm., and the globulin 3.4 gm.

The patient was given a high-carbohydrate, high-vitamin, low-fat diet, with calcium gluconate by mouth and 25 per cent glucose solution intravenously. The course was rapidly downhill, and on the third hospital day the temperature was 104°F., the pulse 130, the respirations 40, and the blood pressure 128 systolic, 66 diastolic. The patient lapsed into coma, cyanosis appeared, and the jaundice intensified, although it was never extreme. Death occurred on the seventh hospital day.

#### DIFFERENTIAL DIAGNOSIS

DR. CHARLES L. SHORT: I think we can dismiss the first attack, which occurred two years before death. At least, I can find no clue there to the cause of death, although of course it is possible that the fatigue

may have been an early symptom of some underlying serious chronic disease.

At the second admission, fifteen months before death, the patient still had the nonspecific complaints of fatigue, nervousness and lethargy, some of which may be assigned to the oncoming menopause. In addition, she had anorexia and vomiting, which point to trouble in the digestive tract. The important diagnostic features at this admission seem to be the large and tender liver, the increased sedimentation rate and the subclinical jaundice, as shown by the van den Bergh test. I should think that the diagnosis of liver disease might at least have been entertained at this time, although there is no mention of it among her discharge diagnoses. I do not believe that we can overlook the increased basal metabolism although only one determination was done. I shall refer to that later.

In the hospital, she developed ketosis from a low-calorie diet. This seems an unusual development and perhaps points to a deficiency of glycogen storage in the liver. Furthermore, if liver disease was already present, this episode certainly was of no benefit to this organ.

On the third admission, the patient obviously had severe liver disease. Again there was an episode of starvation preceding the exacerbation of symptoms, which must have contributed further injury to an already damaged liver. She apparently had a severe anemia. Although the red-cell count was extremely low, the hemoglobin was 65 per cent, thus giving the amazing color index of 2. In the record, there is no description of the smear. At any rate, it seems to have been a hyperchromic anemia, which would go with liver disease.

DR. TRACY B. MALLORY: One smear is recorded: "Some of the red cells appear well filled with hemoglobin; others show considerable variation in size. Many red cells appear larger than normal, and rare stippled cells are present. There are 1 per cent young polymorphonuclears; otherwise the white cells are normal. The platelets are increased."

DR. SHORT: The patient had laboratory evidence at this final admission of severely upset liver function, with an altered albumin-globulin ratio. In spite of treatment, she died in about a week.

I think she obviously had primary or secondary liver disease. With the ascites and the rather rapid final decline, we can probably eliminate biliary obstruction, owing to gallstones or to neoplasm, as a cause of the liver damage. The increased metabolism and the rapid pulse suggest

hyperthyroidism. Decreased liver function has been described secondary to Graves's disease, but it would hardly be as severe as this, and there were no other diagnostic features of hyperthyroidism. There are two other conditions with increased metabolism in which the liver might be involved. These are malignant lymphoma and leukemia. There is no other evidence that I can see for lymphoma, and a leukemia at this stage would probably show some evidence of its presence in the peripheral blood. No bone-marrow studies, of course, were done. A monocytic leukemia might have produced this terminal picture, but I think we shall have to let the increased metabolism go as a single finding that was not confirmed. There is no positive evidence of primary or secondary neoplasia of the liver, although we cannot entirely rule it out.

We are left, then, with some type of hepatitis or cirrhosis. We have already decided against biliary cirrhosis. The facts that the patient was a woman and that there was a lack of pigmentation are against hemochromatosis. However, she did have glycosuria on the third admission, although this may have been due to therapy with intravenous glucose solution. One of the interesting features of this case is the size of the liver, although we know that the clinical estimate of the size of the liver is notoriously inaccurate. If the examiner was able to palpate the liver edge through a fatty abdominal wall and through the ascites, it certainly was a very large liver, with the edge down to the iliac crest. I think that this fact alone is against a toxic cirrhosis, with or without a final episode of acute liver-cell destruction. We ordinarily think of the liver in alcoholic cirrhosis as reduced in size, but this certainly is not always true. I do not believe that a liver even this large is against the diagnosis. This is especially true if the cirrhosis is in the stage, as I believe it may have been, of fatty infiltration, as described by Connor and Chaikoff,<sup>1</sup> rather than being markedly fibrotic. The patient had a history of a consistent intake of alcohol over many years, had been on a restricted diet, and at times had actually been starved. I shall make a final diagnosis, then, of alcoholic cirrhosis, probably in a stage in which fatty infiltration predominated.

DR. WYMAN RICHARDSON: I shall say cancer, if we accept the size of the liver as it is given here. A liver as big as this is *prima-facie* evidence of some form of neoplasm.

I think Dr. Short ought to know whether there was any bile in the stool. Do you know that?

DR. MALLORY: I cannot find a stool report.

#### CLINICAL DIAGNOSES

Cirrhosis of liver?

Ascites.

#### DR. SHORT'S DIAGNOSIS

Alcoholic cirrhosis of liver, in stage of fatty infiltration.

#### ANATOMICAL DIAGNOSES

Acute alcoholic cirrhosis.

Ascites.

Dermoid cyst of left ovary.

Obesity, slight.

#### PATHOLOGICAL DISCUSSION

DR. MALLORY: This is a very alarming story, if one believes it literally, because the patient died of acute alcoholic cirrhosis beyond any shadow of doubt. The liver weighed 4000 gm.—even 5000 gm. is possible in such cases. It was bright yellow, owing chiefly to extensive fat deposit but also to some degree of intrahepatic bile stasis, and very finely granular but quite tough on section—a definite cirrhosis was already present. The liver cells showed the typical so-called “alcoholic hyalin” that one expects in such a case.

If one believes that two cocktails daily for twenty years were really responsible, I think we should all be greatly alarmed. However, we have some evidence, at any rate, that her statements were not entirely reliable. For instance, she swore that she adhered to a 1200-calorie diet, yet she gained over 30 pounds in a year. So that she may have cheated on the alcohol as she did on the food. We did make a few more inquiries afterward, and the results were suspicious although not actually positive: we discovered that gin was bought by the case, and we finally got an admission of at least a case a month. I am still not sure that is the whole story.

The cirrhosis had not advanced to a stage that produced any marked degree of portal congestion. The spleen weighed only 200 gm., scarcely enlarged at all. The amount of ascitic fluid was rather small—only a liter; it was probably due more to the change in level of the serum proteins, that is, the shift in the albumin-globulin ratio, than to the degree of portal congestion.

DR. SHORT: This is probably the first stage of portal cirrhosis?

DR. MALLORY: Yes. One not infrequently observes deaths in an even earlier stage. In large city hospitals and at the medical examiners' table, cases are frequently seen of deaths from acute hepatic insufficiency, showing large fatty

livers with no trace of cirrhosis. Such cases usually have stories not merely of extensive consumption of alcohol but also of virtual starvation so far as food intake is concerned. There is an interesting article by LeCount and Singer<sup>2</sup>—Dr. LeCount was medical examiner for Cook County for many years—on acute hepatic insufficiency as a cause of sudden death. They raised the question whether these deaths might be hypoglycemic, but had no direct proof of it. The livers were virtually devoid of glycogen at autopsy.

A PHYSICIAN: Was there any evidence of gastric hemorrhage?

DR. MALLORY: There was no history of gastric hemorrhage, so far as we know. There were no demonstrable varices. There was a dermoid cyst of the ovary, which had never been discovered.

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a taste for hard liquor, and 95 per cent alcohol became popular as a beverage for the first time. Because of this, bathing alcohol and other forms of denatured alcohol were evolved for home use. As a beverage, 95 per cent alcohol was more hazardous than other alcoholic beverages because of its concentration; as its users became intoxicated they tended to be less careful about its dilution, and the death rate was high. With the repeal of Prohibition, the death rate increased to a still higher level, and there is ample police evidence to the effect that 95 per cent alcohol was, and still is, the responsible agent in a large percentage of cases.

Under the practice before Prohibition, the druggist who obtained a certificate of fitness from the Board of Registration in Pharmacy, for which he paid \$1.00 annually, was authorized to sell intoxicating liquors on the prescription of a physician, and could sell pure alcohol for mechanical, chemical and medicinal uses. The cost of a certificate of fitness has since been increased to \$5.00. With the revision of the laws following the repeal of Prohibition, the requirement that alcohol be sold for mechanical, chemical or medicinal purposes was withdrawn, although it is still sold by druggists with a label indicating this restriction on its uses. Basically, however, the druggist under present-day law is allowed to sell 95 per cent alcohol as a beverage at a cost of \$5.00 per annum for a certificate of fitness. This is special privilege indeed!

The danger of the return of the bootlegger if the privilege of the druggist were restricted is not serious. Massachusetts is the only state permitting the free sale of 95 per cent alcohol by druggists, and yet other states have not unduly suffered from bootleggers.

Finally, it is claimed that physicians would suffer if they were required to write prescriptions for 95 per cent alcohol. In the other forty-seven states there has been no objection on the part of the medical profession to this requirement. In New York, for example, physicians have not complained, and the death rate from alcoholism has been lowered in New York City since the repeal

of Prohibition, in contrast with the increased rate in Massachusetts, notably, in Boston.

If it is granted that the unrestricted sale of 95 per cent alcohol by retail druggists is a privilege, an assumption that the activities and letter of Mr. Silverman seem to bear out, it is difficult to rationalize how the unselfish efforts of physicians such as Dr. Leary and Dr. Moore to abolish, or at least to ameliorate, an indubitable public-health hazard should have received so little support from the legislators of Massachusetts.

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## LOCAL HEALTH DEPARTMENTS

It is beginning to be apparent that local health departments, like most other divisions of human activity, cannot long stand still. Many formerly adequate health departments that tried to drift along have found themselves overtaken during the past decade: for example, one in the vicinity of Boston is now being administered by the head of the welfare department, for better or for worse. The fact that such officials have had no public-health or even scientific training does not disconcert them in the least—they can more glibly recite the incubation periods of communicable diseases than most physicians can. There has often been a gradual shift from physicians who may or may not have been good administrators to administrators who may or may not have been good physicians, and now are finding out that they need not have been physicians at all—just administrators.

The question of how much public-health authority can be safely taken over on a pure administrative basis could be debated at some length: professional and technical assistance is always available; sanitary ordinances are well codified; and the simpler types of milk-route epidemiology are now popularly understood. The public-health worker who rests entirely on these will soon find that he is in nonprofessional competition. A wholesome reaction to this static influence has been the production of well-conceived and well-written reports. A recent excellent example is the *Annual Report* of the Public Health Depart-

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## SALE OF ALCOHOL IN MASSACHUSETTS

MR SAMUEL SILVERMAN's letter, appearing elsewhere in this issue of the *Journal*, criticizes a recent editorial, several of his objections and complaints seem to call for additional editorial comment.

The implication that Mr Silverman and his friends are better psychologists than Dr Moore and his associates is a matter of opinion and needs no discussion.

Mr Silverman claims that alcoholism is an unfair term to apply to those who use alcohol for beverage purposes and who suffer and die therefrom. It has been proved so many times that ethyl alcohol is the toxic agent in alcoholic beverages

which produce intoxication, sometimes with a fatal termination, that this question needs no discussion.

The letter asserts that the statistics and data contained in the former editorial are inaccurate and unfair. The statistics were obtained by Assistant Surgeon General Lawrence Kolb, of the United States Public Health Service, and are obviously authentic. The data with reference to arrests for alcoholism were furnished by the police departments of the respective cities shown, and the death rates by the health departments of the respective cities. Mr. Silverman's quarrel appears to be with a governmental agency and with the police and health departments of Baltimore, Boston, New York, Philadelphia and Washington.

It is said that the data used by Drs. Alexander, Moore and Leary, referring to deaths certified by medical examiners in Massachusetts as directly related to the ingestion of ethyl alcohol, are unwarranted. This attitude undoubtedly arises from the fact that Mr. Silverman, as mentioned above, does not recognize that alcohol, whether imbibed as whisky or as ethyl alcohol, is the toxic cause, directly or indirectly, of the deaths recorded. The proponents of the bill under discussion made no claim that 95 per cent alcohol, as sold by druggists, was the exclusive cause of these deaths.

Mr Silverman warns that restriction against the sale of 95 per cent alcohol by retail druggists would result in the return of the bootlegger and so forth. This acknowledges that the 95 per cent alcohol sold by druggists is used for beverage purposes. The intent of the law was that its use was to be limited to mechanical, chemical or medicinal purposes only, it was not to be used as a beverage.

To understand the situation which obtains with reference to the sale of 95 per cent alcohol by the druggist, a review of recent history is necessary. Before Prohibition, 95 per cent alcohol was used for alcohol baths, the sterilization of thermometers and other such purposes, it was not used as a beverage. Following the Prohibition Amendment, as bootlegging became organized, the smuggling of 95 per cent alcohol was found to be just as easy as that of beer and wine, and much more profitable. The American public developed

a taste for hard liquor, and 95 per cent alcohol became popular as a beverage for the first time. Because of this, bathing alcohol and other forms of denatured alcohol were evolved for home use. As a beverage, 95 per cent alcohol was more hazardous than other alcoholic beverages because of its concentration; as its users became intoxicated they tended to be less careful about its dilution, and the death rate was high. With the repeal of Prohibition, the death rate increased to a still higher level, and there is ample police evidence to the effect that 95 per cent alcohol was, and still is, the responsible agent in a large percentage of cases.

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From 1910 to 1925, he was head of Dr Young's Hospital, which was the only hospital in Arlington at the time he opened it. He was a member of the Massachusetts Medical Society and the American Medical Association.

A son, Dr Kenneth T. Young, a daughter and four grandchildren survive him.

## MISCELLANY

### PNEUMOTHORAX IN PATIENTS OVER FORTY

Of what value is pneumothorax in patients of middle age? Numerous studies of the results and complications attending artificial pneumothorax have been made, but these have nearly all been concerned with patients between the ages of fifteen and thirty-five. Our actual knowledge of the precise merits of pneumothorax in patients over forty is still meager. For that reason, a study (Diamond, S., and Ivey, H. T. Artificial pneumothorax in patients over forty. *Am Rev Tuberc* 43:475-490, 1941) made of World War veterans in whom pneumothorax was instituted merits attention. An abstract of their article follows:

A survey was made of 431 white World War veterans in whom pneumothorax was instituted or attempted after they had passed their fortieth birthday, during a five year period beginning January 1, 1935. Every one of the patients had a positive sputum and a roentgenographically demonstrable cavity at the inauguration of his collapse program. Eighty-one per cent had far advanced disease, 19 per cent had moderately advanced lesions. The disease process was unilateral in 49.3 and bilateral in 50.7 per cent. Fourteen per cent had at least one cavity whose diameter exceeded 4 cm. The average age was slightly under forty-four years—7 per cent were over fifty. The duration of the patients' tuberculosis prior to the attempted induction of pneumothorax ranged from one month to eighteen years.

Patients with apparently permanent closure of the cavities and conversion of the sputums were classed as successful, and these numbered 92, or 20.2 per cent. The unsuccessful numbered 487, and the impossible 311 per cent. The various complications of artificial pneumothorax occurred with no greater frequency than among younger patients. Death was due directly to the complications of pneumothorax in 5 patients. Sixteen of the patients who died had pure tuberculous empyemas, although it is difficult to estimate the degree in which the presence of intrapleural pus contributed to these deaths, for in all cases the pulmonary lesion was actively progressive. Including these 16 cases, the fatalities consequent to complications numbered only 21, or 4.9 per cent of the patients treated, which is about what may be expected in general.

The shorter the time the patient has been ill and the less extensive his lesion, the greater the chances for the success of the therapy and the smaller the probability of occurrence of empyema. Closure of the cavity is effected earlier in patients whose disease history has been brief although pleural effusions—a complication of little significance in most cases—are likelier to supervene in persons who have had tuberculosis only a short time.

The time interval of cavity closure and sputum conversion varies directly with the patient's age; most of the pneumothoraxes became successful in the latter half of

their first year. It seems advisable, therefore, to maintain pneumothoraxes of doubtful efficacy for a longer time in persons over forty than would be wise in younger patients.

Bilateral pneumothorax, properly administered in carefully selected cases, is well tolerated and ordinarily occasions no marked respiratory embarrassment. The surgical division of pleural adhesions is necessary to the completion of the collapse in a large number of persons in the fifth decade, just as it is in younger patients.

Weighing the results and the complications, the authors conclude that artificial pneumothorax is of distinct value in the treatment of patients over forty. It is not so effective as in younger persons, but neither is any other therapeutic measure. Thus far it appears that artificial pneumothorax is enduring in its effects in persons over forty, but final conclusions cannot be drawn until most or all patients in the successful group have been observed for a sufficient length of time after re-expansion to permit accurate estimation of the lasting effectiveness of their pneumothorax.—Reprinted from *Tuberculous Abstracts*, July, 1941.

### RESUME OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JUNE, 1941

DISEASES	JUNE 1941	JUNE 1940	FIVE YEAR AVERAGE*
Anthrax	1	2	4
Chicken pox	11	81	10
Diphtheria	11	6	10
Dog bite	1302	1249	1383
Dysentery bacillary	14	11	17
German measles	535	64	211
Gonorrhea	302	297	304
Lobar pneumonia	207	225	78
Measles	3925	5722	3357
Meningococcus meningitis	16	1	8
Mumps	1114	641	43
Paratyphoid B fever	5	6	13
Scarlet fever	639	3	685
Syphilis	391	339	410
Tuberculosis pulmonary	297	229	291
Tuberculosis other forms	23	24	38
Typhoid fever	7	7	8
Undulant fever	7	3	3
Whooping cough	978	59	599

\*Based on figures for preceding five years.

#### GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from West Springfield, 1 total, 1.

Anthrax was reported from Peabody, 1, West Boylston, 1 total, 2.

Diphtheria was reported from Boston, 5, Fall River, 5, Frammingham, 1, total, 11.

Dysentery, amebic, was reported from Boston, 1, total, 1.

Dysentery, bacillary, was reported from Lynn, 12, Peabody, 1, Russell, 1, total, 14.

Infectious encephalitis was reported from Middleboro, 1, Wintertown, 1, total, 2.

Malaria was reported from Haverhill, 1, total, 1.

Meningococcal meningitis was reported from Boston, 1, Braintree, 1, Brockton, 1, Camp Edwards, 7, Fitchburg, 1, Northbridge, 1, Reading, 2, Weymouth, 1, Worcester, 1, total, 16.

Paratyphoid B fever was reported from Adams, 1, Beverly, 1, Lexington, 1, Salem, 1, Worcester, 1, total, 5.

Pellagra was reported from Boston, 1, total, 1.

Pfeiffer bacillus meningitis was reported from Lancaster, 1, total, 1.

Septic sore throat was reported from Beverly, 3, Boston, 1, total, 4.

ton, 6; Brockton, 1; Cambridge, 1; Fall River, 3; Fort Strong, 1; Newton, 1; total, 16.

Tetanus was reported from: Attleboro, 1; Hingham, 1; Methuen, 1; Quincy, 1; Worcester, 1; total, 5.

Trachoma was reported from: Boston, 1; total, 1.

Trichinosis was reported from: Camp Edwards, 11; total, 11.

Typhoid fever was reported from: Beverly, 1; Boston, 2; Fall River, 1; Haverhill, 2; Springfield, 1; total, 7.

Undulant fever was reported from: Arlington, 1; Lowell, 1; Norfolk, 1; Plymouth, 1; Shelburne, 1; Stockbridge, 1; West Brookfield, 1; total, 7.

Meningococcus meningitis was more prevalent than in any month since May, 1937.

Mumps showed a higher incidence than that in any June since 1936.

The incidence of undulant fever, although lower than that of the two previous months, is the highest for June since reporting began.

Chicken pox, German measles, measles and whooping cough were reported above the five-year averages.

Diphtheria, bacillary dysentery, pulmonary tuberculosis and typhoid fever were at normal levels.

Dog bite, gonorrhea, lobar pneumonia, paratyphoid B fever, scarlet fever and syphilis were reported below the five-year averages.

Only one case of anterior poliomyelitis was recorded during the month.

## CORRESPONDENCE

### "SALE OF ALCOHOL IN MASSACHUSETTS"

*To the Editor:* I am the "paid druggists' lobbyist" mentioned in the editorial appearing in the May 1 issue of the *Journal*, under the caption "Sale of Alcohol in Massachusetts," and I take no offense because of this title since Dr. Merrill Moore and others who were interested in securing the passage of the alcohol prohibition act also employed a lobbyist, but whether he was paid I do not know.

I believe your profession, which your journal reaches, ought to know all the facts pertaining to the attempt on the part of certain physicians to secure the repeal of the present law which permits retail druggists to sell alcohol for medicinal purposes. In the first place, may I state that from my conversations with many physicians I am satisfied that they do not agree with Dr. Moore and the others? Indeed, many psychiatrists are opposed to the position taken by Dr. Moore and the others with reference to the sale of alcohol by retail druggists. I know that Dr. Moore and other psychiatrists are tackling the problem of preventing death from alcoholism from the wrong end.

Psychiatrists are in agreement, I believe, that the question of alcoholism and its effect upon the individual is a personal problem and cannot be solved by a general attack. I am not a psychiatrist or even a physician, but I do believe that the question of treating those who suffer from alcoholism must be individual and not treated as a mass problem. However this may be, I do not believe that the statistics and data contained in the editorial and which were in the main submitted to the Massachusetts Legislature are accurate or even fair. In any event, the Committee on Legal Affairs of the Massachusetts Legislature and the Massachusetts Senate and House of Representatives did not agree with the statistics submitted, as both branches voted against a change in the present law.

I know that doctors will agree with me that "alcoholism" is an unfair term to apply solely to those who use alcohol for beverage purposes. Dr. Moore has very loosely used the statistics relating to alcoholism to apply to alcohol as such. His statistics as to the number of arrests and the number of deaths from alcoholism cannot by any stretch of the imagination be confined solely to alcohol, but undoubtedly refer to alcoholic beverages, which include whisky and other alcoholic beverages. To prevent a greater mortality or insanity from alcoholism, Dr. Moore should come out openly as a prohibitionist to prevent the sale, so far as possible, of all alcoholic beverages or else agree to confine the attack to the individual who suffers from alcoholism. The loose use of the word "alcoholism" by Dr. Moore and others to prevent the sale of alcohol by retail druggists was easily apparent to the members of the Legislature.

The statement accredited to Drs. Alexander, Moore and Leary "that 4505 deaths certified by medical examiners in Massachusetts from 1928 to 1938 were directly related to the ingestion of ethyl alcohol" is absolutely unwarranted and unfair because no one of these doctors has been able to certify that these deaths were directly related to the ingestion of ethyl alcohol as differentiated from other alcoholic beverages. In fact, before the legislative committee there was no defense made by Dr. Moore and the others to the proposition advanced that those patients who were charged with suffering from alcoholism were those who had taken alcohol as well as other alcoholic beverages, and that it was impossible to determine just what alcoholic beverage caused the death of the individual. The comparative statistics in the editorial indicating the number of arrests for intoxication in the various large cities of the United States are indeed misleading and unfair, because the number of arrests for intoxication always depends upon the policy of the police with reference to arrests. For example, in a city like New York very few arrests are made for intoxication because the policy of the police is not to bother with intoxicated persons other than to see to it that they are not harmed, while in other cities, like Boston, such persons are readily arrested. It is obvious that this factor must be considered in determining the number of inebriates, for no rational person will believe that in a given year, New York with a population of 7,000,000 people had only 112 arrests for intoxication, while a city like Boston with a population of approximately 790,000 had 5171 arrests for intoxication. The statistics are so absurd that any intelligent person can appreciate that important factors are missing.

Aside from all this, there is another important phase of the problem which Dr. Moore and his colleagues avoid. They do not answer the proposition that in Massachusetts the restriction against the sale of alcohol by retail druggists would inevitably result in the return of the bootlegger and the use of poisonous alcohol by those alcohol addicts who will be bound to secure their alcohol. So too, will it mean the return of witch hazel, Jamaica ginger, wood alcohol and other types of alcohol drinking, for if the retail druggist is denied the right to sell alcohol, the alcohol addict whom Dr. Moore talks about will resort to every means to secure his alcohol since there will be no avenue available to him because package stores do not sell alcohol. In other words, Dr. Moore would make the cure worse than the disease for the alcohol addict, while at the same time denying to honorable people the right to secure alcohol for medicinal purposes, of which there are many, unless the purchase were made in at least one gallon quantities.



Many physicians have stated to me that they do not want to be compelled to issue prescriptions for those who need alcohol for medicinal purposes, as it would result in a gratuitous service and a bothersome one. The medical profession is so thoroughly in disagreement on this whole proposition that it seems to me that before any attempt for this legislation is made by certain persons who, for reasons best known to themselves and which perhaps it is not necessary to discuss at this time, a more elaborate, substantial and accurate study should be made of the whole problem of alcoholism.

I have read many of the articles which have been quoted repeatedly by Dr Moore and Dr Leary and in most instances these articles refer to alcoholism and the use of intoxicating beverages, and not alcohol as such. We can not legislate morals into the people. That is an individual problem, and the sooner Dr Moore and the others approach this whole subject matter from that viewpoint, the sooner will progress be made.

SAMUEL SILVERMAN, *General counsel*  
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## LICENSE SUSPENDED

To the Editor: The license of Dr Manford R. Spalding, 129 Central Street, Auburn, Massachusetts, was suspended by the Board of Registration in Medicine on July 11 because of deceit in the writing of narcotic prescriptions.

STEPHEN RUSHMORE, *Secretary*  
Board of Registration in Medicine

State House  
Boston

## BOOK REVIEWS

*Medical Genetics and Eugenics*. By Charles B. Davenport A.M., Ph.D., Clyde E. Keeler, M.A., M.S., Sc.D., Maude Slye, A.B., Sc.D. (hon.), and Madge Thurlow Macklin M.D., LL.D. 8", cloth, 141 pp., with 59 illustrations. Philadelphia: Woman's Medical College of Pennsylvania \$1.00.

The six lectures that comprise this book were delivered at the Woman's Medical College of Pennsylvania. These lectures try to show why a trained physician, as guardian of the public health, should have fuller knowledge of the genetic path by which man, the featherless biped who ordinarily talks, has come to his biochemical constitution.

Dr Davenport, the distinguished human geneticist, discusses in the first three lectures the subjects, Human Variability and Mate Selection, Some Social Applications of Eugenics, and, finally, 'Hereditary Relation to Medicine.' Dr Clyde E. Keeler takes up the question, 'The Value of Animal Experiments to the Understanding of Human Genetics,' in which he emphasizes the point that the identity of a great portion of our germ plasm is the secret of why physiologic experiments may be performed on normal dogs, cats, guinea pigs and rats and the findings of these experiments applied to normal man. Dr Maude Slye, in a lecture, 'Genetics and Cancer,' considers her own experimental evidence for the genetic control of the type, the site and the age of cancer. The last lecture, 'The Value of Medical Genetics to the Clinician,' by Dr Madge Thurlow Macklin, discusses actual cases that are of particular value to physicians in the diagnosis and therapy of relatively common conditions.

Throughout these lectures runs the plea for teaching more genetics to medical students and for the creation of an enlightened public opinion regarding genetics.

*Medicine and Health in New Zealand. A retrospect and a prospect*. By Douglas Robb, M.D., Ch.M., F.R.C.S. (Eng.) 8", cloth, 146 pp. Auckland, New Zealand: Whitcombe and Tombs, Limited, 1940. 8/6.

New Zealand seems to be particularly fitting as an experiment station for a social form of medicine. The experiment is already under way, for over three quarters of the hospital beds of all kinds are provided by the hospital boards of the Public Hospital System under the government. The chief weakness of the scheme at present, according to Dr Robb, is a lack of cohesion and correlation. There is no central control, which is essential to the orderly development of hospital work. No major changes have been made since 1910, even though the advance of medicine during the last thirty years should have made many changes imperative. This lack of adjustment to modern trends forms the basis of Robb's provocative book. A new survey of the whole situation is needed before any evaluation of the work of the past can be made or plans for the future laid out. This book contains much of interest for American readers, and no one in the field of social medicine should overlook it.

*The Medical Reports of John Y. Bassett, M.D. The Alabama student*. With an introduction by Daniel C. Elkin, M.D. 12", cloth, 62 pp., illustrated. Springfield, Illinois: Charles C. Thomas, 1940. \$1.50.

Dr John Y. Bassett, the 'Alabama Student' of Osler's delightful essay of nearly fifty years ago, whose fine portrait appears as a frontispiece of the published volume, described his experiences as a country doctor in Huntsville, Alabama, in the *Southern Medical Reports* (1849-1851). These volumes are now so rare that they have been reprinted, with an introduction by Professor Elkin. The story of Bassett's work and his letters from Paris, where he studied after his graduation, are too well known by physicians to need repeating. What is new and of great importance in this edition is an appended letter from Mastin to Osler, received after the *Alabama Student* was first published. In this correspondence, Mastin, who entered Bassett's office in Huntsville as a student of medicine, throws new light on Bassett and his career.

The book, a delightful imprint, sets a high standard for American medical publications. It is a choice item not to be missed by any physician or library.

*The American College of Physicians. Its first quarter century*. By William Gerry Morgan, M.D., LL.D., Sc.D., MACP. 4", cloth, 275 pp., with 36 illustrations. Philadelphia: American College of Physicians, 1940. \$2.00.

The American College of Physicians was founded in 1915 by Heinrich Stern, of New York, with a few physicians of that city. After Stern's death in 1918, the college fell into some disrepute, but reorganization soon took place on a sounder and more national basis. The headquarters were moved to Chicago. The organization grew rapidly. A journal—*The Annals of Medicine*, later called *The Annals of Clinical Medicine*—was established, but internal dissension was rising and friction again nearly wrecked the project. The college was reorganized for a second time, and headquarters were moved to Philadelphia in 1936. In 1940, there were over

4000 members, and it now contains most of the men recognized in the field of internal medicine.

This book, containing the history of the first twenty-five years of the American College of Physicians, is of considerable value as a record of the development of one of the outstanding medical groups in this country. In addition to the history, there are chapters on the constitution and bylaws, a financial record and a note on the publications by the college. The last part of the book is taken up with a chronology of the twenty-five years. The volume contains many small portraits in the text, but there is no list of members or index. The book is badly printed and is issued in the form commonly used by commercial catalogues. The lack of an index is inexcusable. The American College of Physicians is said to have been based on the Royal College of Physicians in London. Whatever the similarity, it is inconceivable that the older institution would have issued a history of its growth in a format so unfitting as this volume.

*Clinical Pellagra.* By Seale Harris, M.D., assisted by Seale Harris, Jr., M.D. With a foreword by E. V. McCollum, Ph.D., Sc.D., LL.D. 4°, cloth, 494 pp., with 66 illustrations, and 4 color plates. St. Louis: The C. V. Mosby Company, 1941. \$7.00.

This book is extremely valuable as an historical résumé of pellagra. It presents in an interesting and readable manner an account of the research done by workers at home and abroad. It is somewhat of an autobiography of the senior author, depicting his progress in the field of pellagra. His familiarity with the disease is graphically expressed throughout the book. His opinions are very frank and interesting, especially when he discusses the various theories of the etiology of the disease.

Attention is called to the environmental background that makes individuals prone to pellagra. Its relation to other diseases is briefly outlined, the discussions on sprue and pernicious anemia being particularly worth while. The chapter on treatment is excellent, outlining in detail the present-day therapy, with many satirical comments on the indiscriminate use of diets and vitamins. The advice on the patient's dietary regime commands attention. The chapter on prevention is admirable.

The book is of value to Northern physicians, especially in these days when there is a tremendous increase in the use of ethyl alcohol. They should become more conscious of pellagra, for there is no doubt that there are more cases in this climate than one realizes. The book on the whole can be profitably read by all physicians. The only comment that might be made by the reviewer is that there is too much repetition, and that the references, although instructive, could be broadened in their territorial scope.

*A Textbook of Clinical Neurology.* By J. M. Nielsen, M.D. 4°, cloth, 672 pp., with 179 illustrations. New York: Paul B. Hoeber, Incorporated, 1941. \$6.50.

This work is an attempt to present a short, complete review of neurology in one volume—an almost impossible task. The subject, like most specialties, has outgrown a single volume, and neurology has increased in the last twenty years beyond the realm of any individual specialist. No man can keep up with the modern literature; much less can he have the time to evaluate it. Kennier Wilson did so reasonably well up to 1935, but his book grew into two large volumes before his death, and some subjects

were incompletely covered. The one-volume, one-man textbook of neurology is probably a thing of the past, and Dr. Nielsen's fine book is an excellent example of the truth of this statement.

The book contains the usual introductory material, with charts similar to those found in many books. The standard diseases are described in the ordinary order, with illustrations of moderate value. What makes the book weak is the lack of evaluation of the literature, and even omissions of certain important additions in the last ten years. The reasons for these shortcomings are clearly stated above: an author cannot be blamed for not completing an impossible job.

For the reviewer, this book will not replace any textbook now at hand. One of the best sections is that on the organic diseases of the brain, which is illustrated by excellent photographs of pathologic sections, particularly gross sections. There is also an excellent chapter on clinical cerebral localization, and another, of less value, on vitamins and avitaminoses. For these sections, the book is of value to the specialist. For students or practitioners, it cannot be particularly recommended.

*Born That Way.* By Earl R. Carlson, M.D. 12°, cloth, 174 pp. New York: The John Day Company, 1941. \$1.75.

This is an unusually interesting biography of a doctor who was born of Swedish parents forty-four years ago. He suffered from a birth injury, which caused cerebral paralysis of the spastic type, with athetosis; awkwardness and stiffness of all four extremities resulted, making life extremely difficult for him from the very start. In spite of his handicap, he went through college and through Yale University School of Medicine, and has made a career for himself by teaching and training children who are similarly affected. He has a school on Long Island and another in Florida.

The book is a well-written story of a dramatic career, and his life illustrates what can be done through persistent effort in overcoming an almost insuperable handicap. It was not easy for him to enter any medical school, and it is greatly to the credit of his medical school that the dean saw in him a man of great promise. The whole world is indebted to him for the splendid example he has set, and for the work that he is doing in helping handicapped children.

*Wolf Child and Humau Child: Being a narrative interpretation of the life history of Kamala, the wolf girl, based on the diary account of a child who was reared by a wolf and who then lived for nine years in the Orphanage of Nidnapore, in the province of Bengal, India.* By Arnold Gesell, M.D. 4°, cloth, 107 pp. New York: Harper and Brothers, Publishers, 1941. \$2.00.

This unique account, based on a carefully kept diary of a missionary and his wife, the Reverend J. A. L. Singh and Mrs. Singh, should capture the attention of all readers interested in the age-old problem of Nature versus Nurture. Dr. Arnold Gesell, founder and director of the Yale University Clinic of Child Development, is of the opinion that this story gives ground for new faith in the stamina of human nature and the potentialities of human growth. There are ten instructive illustrations and a good chronology of Kamala's career as a closing chapter of the book. Students interested in the relations between heredity and environment will find it worth while to see that their libraries contain a copy of this book.

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## THE POTENTIALITIES OF PREVENTIVE GERIATRICS\*

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GERONTOLOGY is the science of aging. Geriatrics may be defined as that special field of medical practice dealing with disease in aged persons. The two must not be confused; the aged are the consequences of aging. The aged are people; aging is a process. Aging begins with the conception of a new individual and continues throughout life. Aging is a part of living, and thus involves both evolutionary and involutional phenomena. Senescence may be defined as that part of the aging process which occurs after the peak of development. Although the changes of senescence are largely involutional, it must not be assumed that all the consequences represent decline. There are important compensatory increments in certain functional capacities. Though long neglected, the unutilized potentialities of the aging and aged are worthy of serious consideration.

Just as geriatrics is concerned with the treatment of disease, preventive geriatrics is interested in the prevention of disease in later life. Probably the most significant period from the viewpoint of prophylactic geriatrics is the two decades from forty to sixty. It is in this period, or even before, that the involutional processes start, later to reveal themselves in the more obvious evidences of aging. Preventive geriatrics does not set as its objective the prevention of aging. To do that would be to arrest life. We cannot stop growing older. But we can hope to modify the consequences of aging and retard the progression of certain factors that make for premature senescence. Although aging is inevitable, the character of growing older is perhaps amenable to modification.

Why is the study of aging so young a science? Surely aging is no new phenomenon. It has continued since the beginning of Time. The age

of the earth has long interested geologists, the age of the universe has puzzled astronomers, and the age of man as a species has been the concern of anthropologists and archaeologists for many years. But the aging of *man as an individual* has received scant attention, and very little, indeed, is known about the basic mechanisms of aging as a biologic process. A young world is interested in youth. Mankind is slowly progressing toward maturation. As culture advances, we are commencing to realize the importance of the elderly.

Although the ancient Greeks delighted in the philosophic discussions of their aged seers, in those days the old were objects of curiosity because of their rarity. In Rome, Cicero wrote his famed *De Senectute* several years before his death at sixty-three. He considered himself an old man in the fifties, and justly so, for few of his contemporaries survived to such ripeness. The average life expectancy at birth for the Roman citizen was about twenty-three years, according to cautious estimates. During the next nineteen centuries, life expectancy increased very slowly. Data from New England in 1850 indicate that life expectancy at birth was but forty years. By 1900, this had risen to forty-eight years for the United States as a whole, and since then the rise has been dramatic. In 1930, life expectancy at birth had increased to about sixty years of age, and it is now over sixty-three for white members of the population.

Looking at the changing picture of humanity from another angle, one sees that in 1900 only 17 per cent of the total population of the United States were forty-five years or older. In 1940, 26.5 per cent were over forty-five, and conservative projection results in the estimate that in 1980—only another forty years hence—more than 40 per cent of the population will be over forty-five years old. Recently released figures from the 1940 census reveal that the median age of the population of this country increased from slightly more than twenty-six years in 1930 to just under twenty-nine years in 1940. This is an increase

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of two and a half years of median age within a decade. At that rate, the median age of the population will be forty-four years in another half century. Furthermore, the number of persons aged sixty-five or more has increased from 6,633,805 to 8,956,206. This is a rise of 36.5 per cent among the elderly, as contrasted with a 7.2 per cent increase in the total population in the last decade.

Such figures speak for themselves. Gerontology is no longer merely academically interesting, but has become an urgent matter in the minds of those sufficiently farsighted to see the handwriting on the wall. The nation is aging rapidly. The virile, violent but short-lived days of physical pioneering are largely past. The future holds promise of profound change. A period of intellectual conquest may be dawning. Man at last lives long enough to have time to think.

The situation is wholly without precedent. Never before in the history of mankind has a like problem presented itself; there are no marked trails to follow. We are almost as ignorant of the potentialities of a maturer mankind as Columbus was of the vast future of this continent. As explorers, we can see but the fringe of a new era, a period fraught with undefined menaces, but likewise presenting vistas of delightful aspect. The children of today will be the elderly of tomorrow. It is our responsibility to explore so far as we are able, to light their way and warn them of dangers, so that this apparent boon of increased longevity does not become a curse. For great longevity without health is not only an individual tragedy, but may develop into a social evil viciously destructive to national economy. Contrariwise, increased longevity of the population can become an incalculably valuable asset to any commonwealth if the potentialities of the elderly are wisely guided.

Urgent and unanswered problems arise in economic, sociologic, political and psychiatric fields as well as in medicine. The direction of some of these problems is already indicated. The clamor of the aged for economic security is heard throughout the breadth of the land. The clamor will become louder. Fantastic schemes are advocated with fanatic vigor and have already taken on political flavor. The problem of employment of older men demands serious and immediate attention, for logic inexorably leads to the conclusion that either the increasing millions of elderly people must have opportunity to work and support themselves or the proportionately dwindling group of younger persons will have to support them in one way or another. One answer implies productivity suited to capacity, the other destructive

costs on what may ultimately become a minority.

Education, which is preparation, has not kept pace with these changes in the social order. Educational curriculums are still geared to the day when life expectancy was fifteen or twenty years less than it is today, when it sufficed that education prepare the boy or girl for the competition of adult life. Neither parents nor teachers have taken cognizance of the necessity for preparation for old age. It has been assumed with complacent smugness that the adult would learn how to grow old—gracefully, happily and usefully—without training or aid. Unfortunately, very few learn this spontaneously. The time has come when educators must revise their objectives. The accomplishments of such men as Oliver Wendell Holmes, William H. Welch, Goethe, Edison, Titian and many others in the evening of their lives are mere indicators of the vast storehouse of latent treasure in those so often sneeringly dubbed "old men." Such careers are rarely fortuitous. Continued development is greatly enhanced by cultivation.

The remarkable increase in life expectancy is attributable largely to control of infectious diseases in childhood and early adult life. This has been accomplished chiefly by the public-health officer and the pediatrician. Through the institution and maintenance of modern sanitation, infant mortality has been dramatically reduced. So-called "summer complaint" was a dreaded disorder of infants that only the older ones among us remember. It passed with the disappearance of contaminated milk and water. Typhoid fever not so many years ago filled the wards of the hospitals in our major cities. Today, it is difficult to find sufficient cases for the teaching of medical students. Cholera, plague, smallpox, diphtheria and scarlet fever are under control through quarantine and immunization. Today, an epidemic of any of these diseases would bring about an immediate condemnation of the health department of the afflicted community. The maintenance of such safety is dependent on unrelaxing vigilance and constant educational activity. The daily hygiene and the nutrition of the people likewise improve under the guidance of continuous dissemination of the knowledge gained by research.

Prophylactic pediatrics has contributed greatly to increasing life expectancy. Not only has there been a vast improvement in the curative therapy of pediatric disease, but the pediatricians have done more than any other group of physicians to advocate and apply individual preventive medicine. By better feeding of presumably healthy ba-

bies and by prophylactic immunization, they have made healthy children healthier. The pediatrician has recognized that health is more than the mere absence of disease, that there are degrees of health. Such prophylactic practices have not only reduced infant and juvenile mortality, but have also unquestionably prevented many chronic sequelae from childhood ills. It is worthy of emphasis to note that marked advances in pediatric knowledge followed recognition of the fundamental concept that the child is not merely "the little man," but presents nutritional, immunologic, functional and structural problems and characteristics peculiar to infancy or childhood or both. A similar focus of attention in connection with senescence presents quite different problems because of specific, though ill understood and less appreciated, structural and functional differences. Thus geriatrics, or the care of the aged, becomes dependent on gerontology, the science of aging.

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Before discussing the application and potentialities of preventive geriatrics, it might be well to orient the problems of gerontology, which are logically divisible into three major categories.

The first is the biology of senescence as a process. Aging is a part of living. The basic biologic processes involve all different forms of life, and should therefore be amenable to study by many disciplines. It must be admitted that ignorance of this subject is profound. Unanswered as yet are such fundamental questions as just what happens to a cell with aging, why aging occurs, what accelerates or retards it, what mechanisms are involved, and why. The elucidation of these basic questions may solve many riddles, among them the riddle of cancer and perhaps that of arteriosclerosis. Scientifically, the cancer problem is but a subdivision of the larger question of aging.

The second category includes the clinical problems of senescence in man, which are clearly divisible into those relating to normal and to abnormal senescence, the latter conditioned by the disorders associated with advancing years.

Normal aging brings many changes, some obvious, others obscure, but all insidious and inevitably progressive. Structural alterations, psychologic changes and biochemical and physiologic differences arise. Normal is not a fixed point but a series of variables that change with age. Chronologic age, as measured in years and months, is not identical with biologic age. Physiologic age varies with each person. The greater the duration of life, the greater the variation. Furthermore, no one ages uniformly throughout, for dif-

ferent structures and systems age at different rates at various times in the life span. At certain ages, the involution of certain structures apparently becomes accelerated. This is illustrated by the rapid thymic involution in infancy and by the quickened regression of the generative organs at the climacteric. Mental aging likewise reveals much individual variation. Because of the complex relation, no single criterion of physiologic age can ever prove feasible.

There is a common misconception that senescence implies decline alone. This is distinctly an erroneous concept, for there is considerable compensatory enhancement of certain functional capacities. For example, loss of physical strength and speed of reaction are often counterbalanced by increased skill and judgment. It has been said that the older mind does not learn readily. The popular phrase, "You can't teach an old dog new tricks," has done immeasurable harm, for it has become so fixed in the minds of young and old alike that its validity is assumed. As a result, many older people admit defeat before trying, and opportunities for adult education are suppressed. Recent and comprehensive studies reveal that once this adult resistance to learning is overcome, the capacity to learn is but very slightly diminished by aging. There is some slowing of the rate but an increase in thoroughness. It would be better to reiterate "It is never too late to learn."

There are many disorders the frequency of which rises sharply with advancing years. The distinctions between the changes of normal senescence and certain of these so-called "degenerative disorders" are not sharply defined. It is most difficult to distinguish certain phenomena of disease from those attributable to aging. The phenomena of disease are, after all, exaggerations of normal reactions and do not imply new mechanisms.

The most significant of these geriatric disorders are cardiovascular renal disease, arthritis, diabetes mellitus, gout, cancer and certain syndromes of the climacteric. Of these, the cardiovascular group, including hypertensive arterial disease and arteriosclerosis, is by far the most significant. Arthritis exacts an immense toll of disability, although its mortality is low. A glance at mortality tables reveals that these diseases so frequent in the latter half of life are replacing tuberculosis, accidents, diarrhea and enteritis as the leading causes of death.

Two characteristics common to all these geriatric disorders are of special concern. First, acute infection plays a negligible role in their etiology. Although chronic foci of infection have long been incriminated as contributing

to the causation of arthritis and play a part in the pathogenesis of certain circulatory and renal diseases, none of these disorders can be classified as infectious or communicable. Secondly, all are chronic and progressive, and usually insidious of onset. The progression is often slow, but it is, nevertheless, inevitably persistent. None are self-limited diseases tending toward spontaneous cure and followed by a protracted period of lowered vulnerability. Rather does the progression of these disorders continuously increase vulnerability to exacerbation and accelerated decline. Cure is, at present, largely beyond hope. The best therapeutics cannot cure hypertensive disease, diabetes, gout or chronic arthritis. Control and retardation of progression are, however, feasible. The adequately controlled diabetic patient is vigorous, active, useful and productive despite the fact that he still has the disease. The earlier in the course of these diseases control measures are instituted, the more effective is the therapy. More can be accomplished with the aging than for the aged.

The problems presented to preventive medicine in the later decades of life differ radically from those encountered with younger age groups. These disorders are not amenable to mass prevention as infectious diseases are. They are not contagious. They are progressive. Thus, preventive geriatrics must become individualized, and it must be applied almost continuously. We cannot immunize a person against hypertensive disease and advise that he report again in two years for revaccination. Furthermore, each case of hypertension requires different therapy for control. No two cases are alike. Individualization must be the keystone of the arch of personal preventive medicine. The control of these maladies requires a totally different approach, and sooner or later these problems will absorb a great part of the time and energies of health officer and practitioner.

The third category concerns the socioeconomic problems introduced by increased longevity, greater life expectancy and the rising median age of the population; they are immense and extremely complex. Industry is just awakening to the implications of the fact that the average age of employees is increasing at a surprising rate. This has been occurring despite the fact that until very recently the vast numbers of unemployed permitted and encouraged the selection of younger workers. In the present emergency, the shortage of trained personnel for technical jobs and the deviation of young men into military training will accelerate the rise in the average age of industrial

workers. War would further speed this rise. Problems of placement, retirement, the utilization and conservation of the health of older men in key positions of great responsibility, the complexities of workmen's compensation laws in relation to occupational exacerbation of pre-existent disease and many more questions are becoming increasingly urgent. Certain problems of adult education have already been mentioned. Problems involving social attitudes toward the aged are distinctly pertinent.

These three major divisions of the problems of gerontology are intimately inter-related. Advance in any one field depends on parallel or preceding advance in the other categories. It cannot be over-emphasized that the more we know about the fundamental biologic mechanisms of aging, the more effectively can clinical medicine treat and understand the aged and aging. Likewise, the greater the clinical knowledge concerning the changing capacities and limitations of older people, the more intelligently can the serious and complex socioeconomic problems be considered. Knowledge, gained by painstaking, tireless and honest research, is the foundation of progress.

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The question arises whether preventive geriatrics is a public-health problem at all. If guardianship of the health of the nation is the function of public-health services, all preventive medicine logically falls within the scope of our responsibilities. As previously suggested, preventive medicine is of two types. These may be called the impersonal or "wholesale" type and the individual or "retail" form of prophylaxis.

Impersonal public-health activities have included the institution and control of modern sanitation, the enactment and enforcement of both local and national quarantine regulations, the control of avoidable hazards of atmospheric contamination and of the physical environment in industry and in schools, public buildings and homes, educational activities in schools and elsewhere directed toward the control of communicable diseases and, last, but not least, the encouragement and application of mass immunization against certain infective diseases. These methods have resulted in magnificent improvement in the health of our youth. However, it is notable that although life expectancy at birth increased fourteen years in the quarter of a century from 1910 to 1935, life expectancy at fifty years increased less than three years. There is reason to pause and consider why the gains have been so asymmetric.

Personal preventive medicine, on the other hand, requires individualized handling of health prob-

lems. Such health-maintenance activities are illustrated by the better student-health services and periodic examinations in industry and to a more limited degree by practitioners of medicine. Included in programs of individual health maintenance must be provision for therapy to control in their incipency the progressive disorders of later life. There are four types of therapy, but we have descriptive adjectives for only three of them: prophylactic therapy, curative therapy and palliative therapy. The fourth is that form of treatment intended to control noncurable disorders and retard their progression. We might temporarily call it "controlative" or "retardive" therapy for want of a better term.

Both these approaches toward health maintenance have their limitations. Impersonal preventive medicine, which has been the mainstay of public-health work in the past, is limited in its effectiveness almost solely to infective and communicable diseases. It is applicable only to groups with a community of interest. It is feasible only with relatively homogenous groups in which a minimum of individualization is requisite. Mass production is effective only so long as the units dealt with are identical or nearly so. With increasing age, individual variability increases. Individuality is a composite of intrinsic and inherited characteristics as modified by the accumulated experiences and vicissitudes of existence. As we age, we each acquire a highly personal set of experiences, mental actions, reactions, infections and intoxications. The greater the age, the greater the variability between individuals.

The limitations of personal preventive medicine as applied to older persons are quite different. In the first place, a great deal of time is required for proper individualization. The early detection of chronic and progressive disorders is more difficult and time consuming than the diagnosis of frank acute disease. The disorders met with in older people are usually asymptomatic in their incipency, when most can be accomplished therapeutically. Frequently, extensive diagnostic and functional studies are necessary to reveal occult defects, which are, nevertheless, significant, for they are often precursors to extensive impairment of health. Furthermore, to prevent, control or retard these disorders, frequent consultations for observation and guidance are necessary. Such work cannot be hurried and requires the highest type of diagnostic acumen. Thus, the practice of individual prophylactic geriatrics is of necessity relatively expensive.

Another and severe limitation to the effectiveness of individual preventive medicine lies in man-

kind's curious perversity in declining to make prophylactic efforts on his own behalf. The best advice is relatively useless if not followed. Impersonal preventive medicine deals largely with matters that require little or no effort on the part of the recipient of the benefits. The city dweller has his sanitary milk and water, his clean food and his protection against communicable diseases without directly participating in the work necessary to ensure these blessings. Personal efforts, often of considerable degree and sometimes involving irksome restrictions, are absolutely essential in the management of early degenerative disorders to retard their progression. Unlike the majority of infectious and acute diseases, chronic disease is not infrequently etiologically associated with indulgence. This is particularly notable in diabetes mellitus, obesity and certain forms of vascular disease.

Another difficulty arises from the fact that although new curative methods of treatment are immediately taken up by both physicians and the lay public, prevention of disease is not regarded as a matter of urgency, and adoption is therefore slow. Geriatric disorders, being insidious and painless in their beginning, are usually neglected; those diseases that hurt early receive prompt attention. With chronic progressive disorders, the patient usually waits until the damage is irreparable, and then expects, nay even demands, that the physician casually shake a miracle from his sleeve. This occurs with such tragic frequency that the physician begins to wonder if pampering paternalism has not erased from the public consciousness the recognition that responsibility for health rests first and foremost on the individual.

Prevention lacks the drama of cure. It is axiomatic that volunteered or free advice is almost never followed. Advice must be sought to be used, and should be paid for if one expects conscientious application. Price as a criterion of value is a misconception that cannot be eradicated in less than several generations. It is extremely difficult to sell prophylaxis. The benefits are revealed only statistically. Statistics are abstractions and thus have very little appeal to the emotions of egocentric mankind. One cannot say, "Do not cross railroad tracks without looking, for you will surely be hit by a train the first time you try it." This is not true. One can say, however, "You will probably live to cross more railroad tracks if you always stop, look and listen. Those who do not, take chances." But those who prefer to take chances, to gamble rather than make an effort, are in the majority.

The greatest obstacle to effective preventive geri-



atics is this inertia. It is not, however, an insurmountable obstruction. Vaccination was introduced against violent agitation. Even today there is much passive and some active resistance to many procedures of preventive medicine. Education is gradually diminishing this resistance, and has often caused parents to seek prophylactic immunization for their children. But education is not accomplished overnight. The course in education to overcome the general inertia of adults toward personal preventive medicine will be a long and arduous program. The deeply ingrained tendency to hear only what we want to hear and see only what we want to see must be combated continuously. And such education must start with the physician, not only as teacher but as student as well. Physicians are proverbially neglectful of their own health and notoriously unmindful of the potentialities of prophylaxis. Let it never be forgotten that example is the first principle of successful pedagogy!

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With the indication why impersonal or community approaches to health maintenance are inadequate to stem the rising tide of disability due to chronic disease among aging adults, the question arises what can be done to facilitate the application of individual prophylactic medicine or preventive geriatrics. Education is the primary step. It is essential that every opportunity be grasped to reiterate and emphasize that health is more than the mere absence of disease. Health has quantitative attributes. Few, indeed, are those who are truly and fully healthy. Physical and mental fitness are not static. Health involves reserves of functional capacities in excess of daily requirements and adaptability to shifting burdens.

The measurement of physical health is fraught with difficulty. Thus far, no one has formulated an adequate minimum routine of examination to reveal the degree of health. Unquestionably, many of our criteria of normality are unsuitable, for there has been but little consideration of age as a variable. The changes of age affect the criteria of health. Arbitrary standards based on chronologic age do not suffice, for biologic age is not necessarily the same as chronologic age. The greater the duration of life, the wider will be the fluctuations between physiologic and chronologic age. The question of how physiologic age may be measured is perhaps the most urgent of all the clinical problems of gerontology. The physician applies that indefinable something we call clinical judgment and arrives at an approximate estimate. There is little precision in such evaluations, however. A logical approach to quan-

titation of biologic age is through the measurement of several functional reserve capacities. Study of several is necessary, for aging does not proceed uniformly throughout the individual. Depletion of reserves occurs long before actual functional failure, when subjective symptoms arise. Such depreciation of reserves is detectable only by the application of controlled stress procedures eliciting responses to increased physiologic work as part of the health inventory. For example, it takes a steep climb to reveal the weak spots of an automobile engine or of an apparently healthy heart. No single observation of normal findings on physical examination can reveal how the body will react under conditions of stress. The pulse rate may be normal at rest, but may rise to excessive heights on effort; the blood pressure may be within normal limits during calm conversation, but may soar to dangerous levels with anger or fear.

Periodic health inventory is the foundation for personal preventive medicine. The term "inventory" is used advisedly, for it is far more comprehensive than the more commonly employed term "examination." The average layman expects an examination to be completed in about half an hour. An adequate health inventory requires much, much longer. A careful, painstakingly detailed history is important. The details of the past are of accumulative value to the physician. Personality plays a major role in personal hygiene for health maintenance. Information gained from laboratory procedures, x-ray studies and functional tests is accumulated and correlated with the other observations. Then, and only then, can the physician evaluate the degree of health of an individual patient. These data make possible the formulation of sound and considered recommendations. It is the prophylactic advice that determines the value of periodic health audits. It is of little profit to the patient if the physician merely records his observations on the card and does not amplify his remarks. Because of this and also because many such inventories are carelessly and superficially conducted, the periodic examination has fallen into disrepute in many quarters. There is no weakness in the principle, but the methods of application have frequently been woefully poor. All too often, the doctor remarks that the patient appears a little "run down" and prescribes a "tonic." This may be equivalent to whipping or spurring a tired horse. To be sure, it makes him go faster for a time, but it hardly helps the horse. The only effective remedy for fatigue is rest.

Rest, to be effective, requires time. Time is a vitally important element to all those concerned with geriatrics. In the first place, time is obviously a factor in aging per se. Secondly, repara-



tive processes are slow, and much more time is required to accomplish the same degree of physical rehabilitation in older persons than in children. Clinical experience shows that a man of fifty may require ten times as long to recuperate fully from an acute infection as a child of five. Therefore, convalescence must be prolonged in proportion to age. The human body has a liberal credit structure on which it may draw in periods of emergency. Violent exertion may lead to an oxygen deficit, which may require some little time for repayment when hyperpnea is continued after the cessation of exertion. Likewise, one may "burn" against the future by "running on one's nerve," by using stimulating drugs, such as caffeine, or by ignoring the warnings of fatigue. Such borrowing is against the tissue reserves of energy and fuel. Sooner or later, these debts must always be paid. With aging, credit gets tighter. Not only is there less margin, but the call for payment becomes more urgent. Fatigue comes on more readily, and more quickly turns into exhaustion. It is increasingly imperative, therefore, that the warnings of fatigue be heeded as we grow older. Preventive geriatric advice should include emphasis on the importance of slowing the pace, avoiding overfatigue and taking sufficient time for recuperation. Thus, the final reckoning may be postponed.

Adequate prophylactic counsel must include many aspects of the patient's life and daily hygiene. The mode of living, adequacy of sleep, character of work, forms and amount of exercise, extent of relaxation and investment of leisure all play parts in the hygiene of health. Careful consideration of the habitual dietary is essential. With older people, the questions of bulk, vitamin intake and fluid balance are particularly pertinent. It is curious how often water is forgotten in considering dietary imbalances. Psychic factors must not be ignored. Many unnecessary anxieties are associated with both the masculine and feminine climacteric, and many avoidable psychic traumas from family attitudes toward the aged may be prevented by timely explanation. Conflicts due to competition with youth at work are frequently benefited by simple airing.

Aging accentuates idiosyncrasies, and certain fads may become ingrained convictions. So long as these dietary or other fads do no harm, it is wisest to leave them alone. The aged person knows quite well what he or she cannot tolerate in the way of specific food aversions. The keynote of all advice to the healthy aging or aged patient is: moderation in all things—in work, play, exertion, food and drink. Much mischief

may be done by sudden and radical curtailment of such habits as the use of tobacco, alcohol or coffee.

If a careful health inventory reveals the beginnings of disease, active therapy should be instituted promptly. As previously mentioned, it is a characteristic of the diseases of late maturity that they are progressive. The earlier retardive or controlative management is applied and the more continuous is the guidance, the better are the results. Although delay in instituting proper therapy on the discovery of an early case of diabetes or hypertensive arterial disease is less likely to have tragic consequences than the neglect of an early case of cancer, this fact never justifies postponement of therapeutic measures. Procrastination permits the degenerative changes to progress to the point where treatment becomes ineffective. It is beyond the scope of the present discussion to consider the principles of active treatment in geriatric medicine.

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There is much that public-health services can do to forward preventive geriatrics. Education of the adult population in the importance of prevention, control and retardation of the chronic and progressively disabling diseases of later life will encourage the seeking of such periodic inventories as those just described. If people request these and are aware of the necessity for comprehensive thoroughness, the services will become available. Today, it is often extremely difficult, even in the larger cities, to find physicians whose primary interest is to maintain health rather than treat disease. Pediatricians are the exception. Yet it is clear that such personal preventive medicine is necessary if we hope to check the ever-increasing numbers of middle-aged and elderly people partially or totally disabled by chronic illness. The economic burden of chronic illness is already a staggering fraction of the total losses due to ill health. Mental disability requiring institutional care must be included in these considerations. It is noteworthy that admissions to state hospitals for mental disease due to cerebral arteriosclerosis jumped in the last twenty-five years from 7.7 to 49 per 100,000 population over forty years of age; this is an increase of over 500 per cent.

Industry is much concerned with these questions, and industrial medicine is in a particularly advantageous position to advance preventive geriatrics. To emphasize the value of adult preventive medicine, it is necessary only to mention that sickness absenteeism of nonindustrial origin is responsible for about twenty times as much lost time as industrial injuries of all sorts. Not only do industrial physicians have the oppor-

tunity to examine hundreds of thousands of new employees each year but also they have the invaluable privilege of examining these same men and women at periodic intervals for many years. The factory stands in much the same relation to many adults as the school holds in relation to children. The role of the school physician and school nurse in developing prophylactic pediatrics was and is most significant. A similar opportunity to develop and apply prophylactic geriatrics awaits industrial physicians and nurses. Divisions of industrial hygiene in health departments can do much to encourage the expansion of such activities. Prophylactic geriatrics does not start at any particular age; health in maturity is good insurance toward healthy old age.

There remains for brief discussion the greatest and most important service that public health can offer the older fraction of the population: research into the problems of aging. Here the field is so wide, so untrammled and so unexplored that the potentialities are truly without end. I have deplored our ignorance of the fundamental biologic process of senescence. Badly needed are accurate and controlled studies to reveal what actually happens with aging. Cytologic, biochemical and physiologic definition of the changes that are part of normal aging are necessary as base lines on which to place evaluation of what constitutes "normal" in relation to age. The relations of age to growth and growth potentials, the changing vulnerability of cells to noxa and to pharmacologically active substances urgently require illumination. Nutritional requirements and tissue respiration in relation to age are fertile fields for study, and are ready for cultivation. The etiology and pathogenesis of arteriosclerosis, hypertensive arterial disease and cancer have obvious but ill-defined relations to the aging process.

Clinical researches are needed just as urgently. Only a few of the many unanswered questions clamoring for solution are the problems of how to evaluate physiologic age in man, and the definition of the curves of "normal" in relation to age. Such knowledge is prerequisite to studies of most geriatric diseases. Present clinical methods of functional mensuration need critical appraisal, and new, more precisely controlled, stress-test procedures are wanted. Any advance in knowledge concerning the so-called "degenerative diseases"

advances geriatrics, but we must not forget the lesson learned from pediatrics, namely, that the greatest advances were made when the peculiar structural, biochemical and physiologic characteristics of the infant and child became more clearly defined.

The socioeconomic problems of the aging population are not beyond the ken of public health. The problems of industrial health, housing, optimum nutrition and old-age assistance and the costs of chronic illness, chronic-disease hospitals and the maintaining of mental health are all borderline questions.

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In brief recapitulation, it should be emphasized that the three major categories of problems, the biology of senescence, the clinical questions of aging man and the socioeconomic problems, are all intimately related. Advance in one field will be immediately reflected by progress in the others. The more we know concerning the fundamental processes of aging, the more effective can clinical geriatrics become; the more precisely clinical medicine can define the changes in capacities and limitation that occur with normal aging and the more effectively it can apply preventive geriatrics, the more intelligently can the socioeconomic problems be attacked. These three divisions cannot be arbitrarily separated. Comprehensive programs of research must consider the field as a whole.

Prophylactic geriatrics does not take as its primary objective the prolongation of life. Rather, in the words of George Morris Piersol, does it aim to "add more life to the years rather than more years to life." By understanding and developing the capacities of older persons, it can help them to remain useful much longer. There is no greater tragedy for the aged than the sense of uselessness that society today prematurely imposes on them.

It must not be forgotten that the posts of greatest responsibility, requiring the highest judgment, technical training and wisdom, are held by older men. And with good reason. The accumulated judgment and wisdom of these older minds represent one of the most valuable and potent resources of the nation. The conservation of the health and vigor of these almost irreplaceable older men is a major potentiality of preventive geriatrics.

# CERTAIN OBSERVATIONS IN LOW-NITROGEN, NORMAL-OXYGEN ATMOSPHERES RELATED TO THE PROBLEMS OF HIGH-ALTITUDE FLYING\*

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IN the course of studying the effect of low-nitrogen, normal-oxygen atmospheres on the dyspnea of obstructed breathing,<sup>1</sup> observations were made on the effects produced by such atmospheres that bear directly on the problems of high altitude flying. Because these effects have become of particular importance in current aerial warfare and in low atmospheric-pressure experiments pertaining thereto, publication of our findings seems desirable.

The experiments were conducted in a steel chamber,<sup>||</sup> which consisted of two rooms. In each room, controls by suitable pipes and valves were made so that from either inside or outside the pressure chamber the room could be evacuated rapidly and almost noiselessly by means of a steam ejector to any desired extent and could be refilled with room air or oxygen as desired. A bank of oxygen tanks was provided with a reduction valve so that an adequate source of oxygen at a pressure of 50 to 100 pounds was available. Cooling of the chamber was effected by a coil carrying brine. The accumulation of carbon dioxide was prevented by frequent small reductions of total pressure and additions of oxygen and air. Convection currents facilitated the absorption of carbon dioxide by a container of soda lime. Water pipes to each chamber provided the essential fire-extinguishing equipment.

By repeating the process of alternately lowering the total atmospheric pressure until the partial pressure of oxygen was reduced to approximately 125 mm of mercury and then increasing the partial pressure of oxygen to approximately 225 mm, a total atmospheric pressure of 200 mm (corresponding to an altitude of approximately 32,000 feet) and a partial oxygen pressure of 155 mm

could be provided within the chamber in ten minutes. A fairly accurate account of the oxygen pressure was kept by calculation from the pressure changes. An accurate check was made at intervals by direct oxygen analysis, which took but two or three minutes.

From observations during experiments at low-nitrogen, normal-oxygen atmospheres, Mosso,<sup>2</sup> Winterstein,<sup>3</sup> Fegler<sup>4</sup> and Dill, Edwards and Robinson<sup>5</sup> postulated an excess carbon dioxide elimination that was not dependent on the hyperpnea of anoxemia. Ruhl<sup>6</sup> found that the slight lowering of the carbonic acid of arterial blood in such atmospheres was accompanied by a compensatory de-

TABLE 1. Alveolar Oxygen and Carbon Dioxide Pressures and Percentage Saturation of Hemoglobin at Atmospheric Pressures Corresponding to Various Altitudes When the Atmospheric Oxygen Pressure Is Maintained at the Sea Level Value

ALTITUDE	ATMOSPHERIC PRESSURE		CALCULATED ALVEOLAR OXYGEN PRESSURE		OBSERVED ALVEOLAR OXYGEN PRESSURE		OBSERVED ALVEOLAR CARBON DIOXIDE PRESSURE		CALCULATED ALVEOLAR HEMOGLOBIN SATURATION	
	mm Hg	mm Hg	mm Hg	mm Hg	mm Hg	mm Hg	mm Hg	mm Hg	%	%
0	760	159	104	100	100	40	98	98	100	98
6,000	500	150	94	105	105	40	96	96	96	96
11,000	304	156	96	112	112	39	97	97	97	97
17,000	400	156	93	100	100	37	95	95	95	95
19,000	360	158	93	87	87	40	95	95	95	95
23,500	300	156	87	84	84	37	94	94	94	94
27,700	250	156	81	79	79	39	93	93	93	93
32,500	200	159	67				92	92	92	92
37,500	159	159	67				90	90	90	90
40,000	140	140	48				80	80	80	80

\*Assuming a constant alveolar vapor pressure of 48 mm of mercury, a carbon dioxide pressure of 40 mm, a respiratory quotient of 0.9 and no hyperpnea.

$$\text{Alveolar oxygen pressure} = (\text{atmospheric pressure} - \text{water vapor pressure}) \times \frac{\text{partial oxygen pressure}}{\text{atmospheric pressure}} - (\text{alveolar carbon dioxide pressure} \times \frac{1}{0.9})$$

†Determined from the calculated alveolar oxygen pressure.

crease in bicarbonate and no change in the pH of the blood. Armstrong<sup>7</sup> in similar atmospheres observed no abnormal elimination of carbon dioxide.

Table 1 presents our observed and calculated<sup>†</sup> alveolar oxygen pressures at total atmospheric pressures corresponding to varying altitudes, when the atmospheric oxygen pressure was maintained at the sea level oxygen pressure of 155 mm. of mercury. The relative constancy of the alveolar car-

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||The plan of the chamber was conceived by Dr. James L. Wilson. Its construction was supervised by Dr. Wilson and Professor Philip Drinker of the Harvard School of Public Health.

bon dioxide pressures over this range in altitude does not indicate an abnormal elimination of carbon dioxide. That there was no significant alkalosis due to abnormal loss of carbonic acid from the blood is indicated by the fact that there was no increase in urine volume or alkalinity such as would accompany a respiratory alkalosis.<sup>8</sup> Thus our results do not indicate that in rarefied atmospheres there is a significantly increased elimination of carbon dioxide that is independent of the hyperpnea of anoxemia.

Fegler<sup>4</sup> and Dill and his co-workers<sup>5</sup> believed that the greater elimination of carbon dioxide observed by them at low pressures resulted from the greater diffusion of carbon dioxide from the alveolar spaces to the pulmonary dead space when the air in the lungs was reduced in density. It has

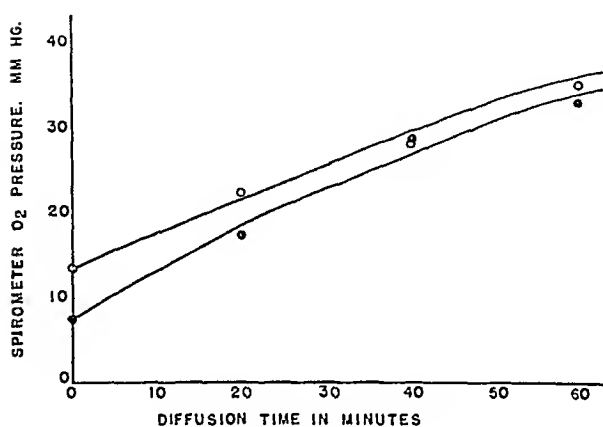


FIGURE 1.

*This chart shows the rates of diffusion of oxygen into a spirometer at a constant partial oxygen pressure of 150 mm. of mercury at total atmospheric pressures of 760 mm. of mercury (open circles) and of 300 mm. of mercury (solid circles).*

similarly been suggested<sup>9</sup> that an acceleration of the diffusion rate of oxygen at low-nitrogen pressures facilitates respiration. To obtain data on the diffusion of oxygen at atmospheres of varying density, a large spirometer was filled with nitrogen after the oxygen of the dead air space of the apparatus had been washed out with nitrogen. The spirometer was then opened to the surrounding atmosphere by removing the two corks at its base, thus allowing two apertures each about 2 cm. in diameter. At the beginning of each experiment and at intervals thereafter, samples were drawn off for quantitative analysis of oxygen content. Such experiments were conducted at sea-level pressure with room air and at 300 mm. of mercury total pressure, with a partial pressure of oxygen of 150 mm. Figure 1 gives the partial pressure of oxygen plotted against the diffusion time in min-

utes. The curves show a similar rate of diffusion at the two atmospheric pressures. This suggests that acceleration of the diffusion rate of oxygen does not significantly facilitate respiration at low-nitrogen pressures.

Bert,<sup>9</sup> Boycott and Haldane<sup>10</sup> and Haldane<sup>11</sup> called attention to the theoretical possibility of "bends" if the atmospheric pressure was reduced too rapidly from that of sea level to 300 mm. of mercury or less. Von Schrötter<sup>12</sup> recorded symptoms resembling "bends" after reduction of the total pressure in a tank to 230 mm. in fifteen minutes but believed the symptoms could not have been "bends." In experiments in which the pressure was reduced rapidly to 250 mm. or less, we observed on several occasions one or more of the following symptoms: joint, muscle, precordial and thoracic pains, rapidly spreading skin anesthesia and scotoma. Since then, Armstrong<sup>7</sup> has reported similar experiences. At pressures of 250 mm. of mercury or less, we regularly observed a burning sensation of the eyes and tingling and other paresthesias of the skin. At such pressures, we were also aware of an increase in the effort required for physical and mental work. Inertia prevented a ready response to any task. Armstrong has likened this to the symptoms of anoxia without anoxemia. These symptoms observed independently by Armstrong and ourselves and Armstrong's evidence<sup>7</sup> concerning the formation of nitrogen bubbles and the occurrence of increased intracranial pressure indicate that the possibility of decreased-pressure disease, that is, "bends" and increased vaporization of body water, is a real danger. Although preparatory elimination of nitrogen by breathing oxygen prior to ascent lessens the danger of "bends," this precautionary procedure will not remove the danger that may accompany the increased vaporization of body water at low atmospheric pressures.

Armstrong and Heim<sup>13</sup> have given an excellent description of the adjustment of pressure within and without the middle ear during ascent and descent. In ascent, the expanding air in the tympanic cavity automatically escapes through the eustachian tube. In descent, however, the increasing external pressure closes the eustachian tube, and equilibrium can be established only by opening the tubes by voluntary contraction of their dilator muscles. If the differential pressure becomes greater than 90 mm. of mercury, the muscles can no longer open the closed tubes, and the ready establishment of equilibrium becomes impossible. A differential pressure of 30 mm. causes pain, and an increase in the differential external pressure of 100 mm. or more usually results in rupture of the eardrum. In our experi-

ence, the readiness with which closing of the eustachian tubes accompanied rapid descent varied greatly with the subject, and was also dependent on whether or not congestion and inflammation of the mucous membrane of the nasopharynx were present. Certain subjects encountered great difficulty in preventing closure of the tubes by the usual procedure of swallowing and yawning, even during relatively slow descent, whereas others encountered no difficulty with very rapid descent.

Preliminary observations on the burning of matches and cigarettes revealed a marked increase in their rates of combustion at low-nitrogen, normal-oxygen pressures. With the aid of Professor Philip Drinker, a controlled series of experiments on the rate of burning of carefully calibrated candles was carried out in atmospheres of different nitrogen pressures but with a constant partial pressure of oxygen of 150 mm. of mercury. The results are plotted in Figure 2. This increased rate of combustion at the low-nitrogen pressures introduces a fire hazard that deserves consideration and seems to have been overlooked by other workers. Our data suggest that pressure chambers for low-pressure experiments or pressure-

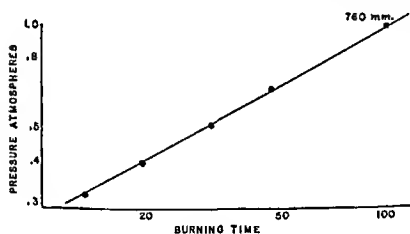


FIGURE 2.

*This chart shows the increase in rate of combustion or decrease in burning time with a decrease in total atmospheric pressure but a constant partial-oxygen pressure of 150 mm. of mercury. The scales of ordinate and abscissa are logarithmic.*

cabin planes for high-altitude flying should be equipped with adequate fire-extinguishing equipment that will withstand the pressure changes and will not liberate toxic gases.

Finally, the low values for alveolar oxygen observed at total pressures of 250 mm. of mercury or less, in spite of the adequate partial pressures of oxygen, demonstrate a limit to high-altitude flying unless the total atmospheric pressure, as well as the partial pressure of oxygen, is maintained above certain limits. In Table 1, the calculated alveolar oxygen and arterial hemoglobin saturation have been extended to total pressures below, and thus

to altitudes above, the levels at which the alveolar air was actually determined. The risk involved in handling mercury in a closed chamber at markedly reduced pressures, owing to the marked increase in vaporization, was one of the factors that limited our analytical experiments. The data demonstrate that at altitudes above 32,000 feet or at total pressures below 200 mm. of mercury the alveolar oxygen and arterial hemoglobin saturation fall off significantly and with increasing rapidity, in spite of a partial-oxygen pressure of 159 mm. This is accounted for by the normal alveolar carbon dioxide and water-vapor pressures of 40 and 48 mm., respectively. At a total pressure of 140 mm., the sum of these normal alveolar carbon dioxide and water-vapor pressures permits, even if pure oxygen is breathed and the respiratory quotient is 1.0, an alveolar oxygen pressure of but 140 mm. minus 88 mm., or 52 mm., of mercury unless hyperpnea is present. This pressure is not very much above the normal venous oxygen pressure of 40 mm. of mercury. Hyperpnea increases the alveolar oxygen pressure, but unless the atmospheric carbon dioxide pressure is increased, results in decreased alveolar carbon dioxide pressure and alkalosis. An atmosphere of pure oxygen at a total pressure of 130 mm. of mercury or an altitude of 42,000 feet would probably result not only in the same potential dangers due to anoxemia as are encountered in ordinary air at 22,000 feet but also in the dangers due to reduced-pressure disease. Indeed, a recent report by Ceres<sup>14</sup> suggests that effects of the latter are encountered in flights above 30,000 feet.

Thus, to reach altitudes greater than 32,000 feet with any degree of safety, provision must be made for controlling not only the partial pressures of oxygen but also the total atmospheric pressure. This requirement, the middle-ear disturbances in descent, the possibility of "bends" in ascent and of increased vaporization of body fluids at very high altitudes, and the fire hazard at low-nitrogen, normal-oxygen pressures result in great vulnerability at altitudes much beyond 35,000 feet.

#### SUMMARY

Observations related to problems of high-altitude flying made during experiments at atmospheric pressures of 250 to 200 mm. of mercury, corresponding to altitudes between 28,000 and 32,000 feet, are presented and discussed. The increased rate of combustion observed in low-nitrogen, normal-oxygen atmospheres is such as to cause a fire hazard that deserves careful consideration and precautions.

We are indebted to Professor Philip Drinker, Mr. Charles Miller and Miss Elsie MacLachlan for their co-operation and assistance in the course of these experiments.

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## CHRONIC GASTRITIS: A GASTROSCOPIC AND CLINICAL STUDY\*

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THIS communication reports the results of studies of chronic gastritis in adults, the diagnosis of which was made by means of gastroscopy. There were three purposes for making these studies. The first was an investigation of the symptomatology, including an analysis to ascertain whether certain symptoms would permit a presumptive diagnosis of chronic gastritis before performing gastroscopy. The second purpose was to collect statistics on the incidence of chronic gastritis, as observed gastroscopically. A third was an attempt to discover whether the existence of chronic gastritis in the presence of peptic ulcer influenced the symptomatology of the latter condition.

Schindler<sup>1</sup> has developed a practical classification of the main types of chronic gastritis based on gastroscopic studies. An elaboration of this classification, suggested by McClure and Jankelson,<sup>2</sup> embraces the various types of chronic gastritis observed in over 1000 gastroscopic examinations. This classification comprises three main types: the superficial, the atrophic and the hypertrophic, each of which may occur as the simple, ulcerating or hemorrhagic form. Except for the superficial, these terms are self-explanatory. The superficial type is a chronic gastritis in which the mucosa appears inflamed, with redness, swelling and edema and an excess of mucus. The above classification will be followed in describing our observations.

The pathologic characteristics of various types of gastritis were first established by the post mortem studies of Faber<sup>3</sup> His findings were subsequently confirmed by the extensive observations of Konjetzny<sup>4</sup> on gastric mucosa resected during laparotomy, and more recently by Eusterman,<sup>5</sup> Schindler<sup>6</sup> and others However, the practical clinical diagnosis of gastritis was not possible until the development of the Wolf Schindler semiflexible gastroscope in 1932 This instrument permits the direct visualization of mucosal changes such as the various types of chronic gastritis, erosions, superficial ulcerations, purpuric manifestations and other lesions of the gastric mucosa not otherwise readily demonstrable during life As a result of the use of this gastroscope, a large literature on

gastroscopic findings has accumulated and has been correlated by Schindler,<sup>1</sup> Swalm, Jackson and Morrison,<sup>7</sup> Swalm and Morrison,<sup>8</sup> Schindler and Murphy<sup>9</sup> and in reviews by Cheney,<sup>10</sup> by Jones et al,<sup>11</sup> and by others. All the observers agree that chronic gastritis is a common gastroscopic finding. This frequency is well illustrated by Schindler's<sup>12</sup> tabulation of the gastroscopic findings in 1000 patients, in whom the lesion was present in 42 per cent, Carey<sup>13</sup> found it in 44 per cent of 700 gastroscopies. Nevertheless, more recently Ruffin, Brown and Clark<sup>14</sup> conclude from the results of their gastroscopic observations that the reported frequency of chronic nonspecific gastritis is to be seriously doubted.

Most of the reported gastroscopic studies have been largely concerned with descriptions of the gross anatomic changes observed, and but incidentally with the accompanying symptomatology. How little differential diagnostic knowledge has been accumulated is illustrated by a quotation from Swalm et al.,<sup>7</sup> "The symptoms of gastritis are so variable that they range from a complete absence of symptoms to flatulent dyspepsia to perfect mimicking of peptic ulcer with its hunger pains and food or alkali relief with hematemesis." Nevertheless, more recent studies<sup>9 15-17</sup> suggest the possibility of clarifying the symptomatology. These studies indicated that in patients with gastritis the appetite was often poor, although it might remain unaffected but was not found to be increased. Relief after food was found to be less common than in ulcer, indeed, food not infrequently aggravated the symptoms. Epigastric distress or true pain was the rule and was often of the delayed type. Severe epigastric pain, not referred, was reported only in the hypertrophic form.<sup>15</sup> Hemorrhage was an important complication.<sup>1 15-20</sup> It was suggested<sup>9</sup> that the atrophic type may be differentiated by the general symptoms of marked weakness, sense of fatigue, emotional depression, sore tongue and paresthesias. Although the degree of gastric acidity was reported<sup>9 15 21</sup> to be variable, achlorhydria or hypoacidity was more commonly found in the atrophic type and normal or increased values in the superficial and hypertrophic forms.

The incidence of any pathologic condition is always of great importance. For this reason, we determined the frequency of chronic gastritis by means of gastroscopic observations in 611 consecutive patients; it was present in 269, an incidence of

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44 per cent. Although 99 (37 per cent) of these patients showed mixtures of the different types of gastritis, in each of them one type predominated sufficiently to permit a classification as essentially hypertrophic, atrophic or superficial. On this basis, 150 (56 per cent) were of the hypertrophic, 51 (19 per cent) of the atrophic, and 68 (25 per cent) of the superficial type, an incidence of 25 per cent, 8 per cent and 11 per cent, respectively. The findings are comparable with those reported by other observers,<sup>11,14</sup> and show that various types of chronic nonspecific gastritis are of common occurrence. The associations of the types of gastritis mentioned above were hypertrophic with superficial in 33 cases, hypertrophic with atrophic in 29 cases, atrophic with superficial in 25 cases, hypertrophic with superficial and atrophic in 4 cases, and ulcerating or hemorrhagic ulcerating with either hypertrophic or atrophic in 8 cases. These figures represent incidences of 5.4, 4.7, 4.1, 0.7 and 1.4 per cent, respectively.

For the purpose of evaluating the symptomatology of chronic gastritis, 75 patients were subjected to comprehensive studies. Obviously, the thoroughness of such studies is an essential factor governing their value. For this reason, with certain exceptions, all observations and procedures incident to the clinical study were carried out with the utmost care by at least one of us; and in every case gastroscopic examination was made by two of us. The exceptions mentioned refer to the radiographic and laboratory procedures, the majority of which were performed in the appropriate departments of the hospital.

The clinical studies showed that a small number of patients were troubled with constipation, but in most of them the bowel habits were not unusual. Weight loss was sustained by 6 patients with hypertrophic and by 4 with atrophic gastritis. The loss was approximately at the rate of 1 pound a week and was never extreme. Twenty-nine of the patients with hypertrophic and 25 with atrophic gastritis showed no weight loss. Thus, changes in weight in this series of patients were not of clinical importance. Except as the result of gross hemorrhage, the blood and stools showed nothing demonstrably abnormal. The Hinton test on the blood serum was negative in all the patients, as was the usual clinical examination of the urine.

Thirty-nine of the patients presented hypertrophic gastritis, and 29 atrophic gastritis. Of the former, 34 were men and 5 women, whereas of the atrophic, 17 were women and 12 men. Thus, men predominated greatly in the hypertrophic and women to a lesser extent in the atrophic type.

Table 1 shows that the ages varied from twenty to eighty years, with a rather even distribution of the hypertrophic cases for each decade; the atrophic type showed lessened incidence in the sixth and eighth decades. However, in general the

TABLE 1. *Ages of Patients.*

AGE yr.	NUMBER OF PATIENTS	
	HYPERTROPHIC GASTRITIS	ATROPHIC GASTRITIS
20 to 30.....	6	7
30 to 40....	5	7
40 to 50.....	8	5
50 to 60.....	8	2
60 to 70.....	10	7
70 to 80.....	7	1

age incidences found for the two types of gastritis are comparable.

The duration of the symptoms for both types of gastritis is outlined in Table 2. In general, the duration was comparable in each group. This tabulation also indicates that gastritis is a chronic condition.

Of the 68 patients showing hypertrophic or atrophic gastritis on gastroscopy, 20 had a duodenal ulcer and 1 a gastric ulcer, as diagnosed by

TABLE 2. *Duration of Symptoms.*

DURATION	NUMBER OF PATIENTS	
	HYPERTROPHIC GASTRITIS	ATROPHIC GASTRITIS
Less than 1 yr. ....	4	8
1 to 5 yr. ....	16	10
5 to 10 yr. ....	3	6
10 to 15 yr. ....	6	1
15 to 20 yr. ....	3	1
20 to 25 yr. ....	7	1
25 to 40 yr. ....	0	0
40 to 45 yr. ....	0	2

x-ray studies, and 6 presented x-ray evidence of gall-bladder disease or had undergone cholecystectomy. The presence of the gastric ulcer was verified by gastroscopic observation. The remaining 41 cases were uncomplicated; an analysis of the symptomatology of these patients is given in Table 3. Of the 41 patients with uncomplicated chronic gastritis, 30 complained of epigastric discomfort or mild pain, and 9 of severe epigastric pains. Thus, epigastric discomfort and pain were the commonest symptoms. As the table shows, they were variably related to the time of taking food, and they were also variably relieved by the ingestion of food or alkali. The peptic-ulcer characteristic of periodicity of symptoms was described by 24 of the patients. Good appetite was present in 32, and anorexia in 12. Vomiting was a prominent symptom in 15, and hematemesis in 5. Of the 2 patients with atrophic gastritis without pain



or discomfort, one complained of nausea and fatigue and the other complained of fatigue and also of the regurgitation of small amounts of bloody liquid. Fatigability occurred in 33 per cent of the atrophic, but was absent in the hypertrophic group.

The data correlated in the table are the results of careful scrutiny of each patient's history. They indicate the basis for concluding that, except for fatigability and absence of epigastric complaint in 2 patients of the atrophic group, the symptomatology of hypertrophic and atrophic gastritis is similar. The case scrutiny also disclosed that 10

TABLE 3. *Symptomatology of 20 Hypertrophic and 21 Atrophic Cases of Uncomplicated Chronic Gastritis.*

SYMPTOM	NUMBER OF PATIENTS	
	HYPERTROPHIC GASTRITIS	ATROPHIC GASTRITIS
Severe epigastric pain	2	-
Mild epigastric pain or discomfort	13	-
Constant or intermittent pain	10	7
No time relation of pain to meals	15	10
Pain augmented by food	6	1
Pain or discomfort relieved by food	16	11
Pain or discomfort relieved by alkali	17	9
Periodicity of symptoms, like ulcer	11	13
Symptoms typical of ulcer	5	5
Good appetite	18	14
Anorexia	7	5
Vomiting	9	6
Hematemesis	3	2
No epigastric pain or discomfort	0	2
"Nervousness"	7	9
Fatigability	0	9

patients in these two groups showed symptoms characteristic of peptic ulcer. An analysis of the symptomatology of the remaining 31 cases shows certain symptoms differing from those of the typical peptic-ulcer syndrome: no time relation of pain or discomfort to meals, 25 cases; pain or discomfort augmented by food, 9 cases; pain or discomfort not relieved by food or alkali or by both, 5 cases; constant or intermittent pain or discomfort, 17 cases; constant pain or discomfort not relieved by food and associated with sharp, knifelike epigastric pain definitely related to meals, with relief by alkali, 6 cases; anorexia, 12 cases.

Of the 21 patients showing both chronic gastritis and ulcer, modification of the usual ulcer syndrome occurred in 4. In 3, duodenal ulcer was present; of them complained of anorexia, the second had anorexia, with no relief by food, and the third, in addition to these symptoms, stated that there was no time relation between the onset of pain and food intake. The fourth patient, who had a gastric ulcer, experienced no relief from pain after either food or alkali.

The presence of chronic gastritis caused no demonstrable influence on the symptoms presented by the 6 patients with chronic cholecystitis or by those who had undergone cholecystectomy.

In this study, x-ray observations were found to be of inconsequential value as a direct aid in the diagnosis of gastritis. However, barium gastrointestinal x-ray studies were of essential value in determining the presence or absence of esophageal lesions, cancer, ulcer of the stomach, pyloric obstruction, duodenal ulcer and lesions elsewhere in the small or large bowel. Radiography was of similar value in relation to the diagnosis of diseases of the gall bladder.

## DISCUSSION

Chronic gastritis is known to be a common pathologic entity; it was observed gastroscopically in 44 per cent of our patients and in comparably high percentages by others.<sup>12, 16</sup> These high incidences resulted from limiting observations to those patients presenting gastric complaints. For this reason, the findings do not denote the frequency in the general population. The latter may be calculated by the use of the mean average of figures reported by the Commission on Medical Education,<sup>22</sup> which shows that 13.4 per cent of all patients visiting outpatient departments present digestive complaints. If gastroscopy reveals chronic gastritis in 44 per cent of these cases, the incidence among the general population is approximately 6 per cent.

The types of gastritis can be divided into primary and secondary groups.<sup>2</sup> The latter group includes chronic gastritis occurring in the course of either an established causal or a possibly causal pathologic condition. In our cases that were carefully studied clinically, 34 (45 per cent) accompanied peptic ulcer or gall-bladder disease. This finding confirms the conclusion drawn from a much larger number of less carefully controlled observations that the condition is a secondary entity in 50 per cent of the patients in whom it is observed. On the basis of this percentage, proper calculation shows that the incidence of primary chronic gastritis among the general population is about 3 per cent. In the aggregate, this percentage represents a large number of patients. Furthermore, the results of the present investigation and those of other observers<sup>16-17, 23</sup> show that it is a chronic disturbance, causing mild to serious and even incapacitating disability. It is also established that the condition is not infrequently mistaken for peptic ulcer, whereas it may be confused with carcinoma of the stomach,<sup>6, 24</sup> which has caused useless laparotomies.<sup>24</sup> Thus, chronic gastritis affects a sufficiently large number of patients to make its clinical investigation very important.

Morphologically, primary gastritis is indistinguishable from the secondary type, and clinical

studies furnish the only means of differentiation. Obviously, without this differentiation, the symptomatology may include a variety of manifestations due to a causative primary disease. For this reason, the analysis in this communication represents the findings only in those patients who have been intimately studied and observed for a prolonged period. This explains why the findings are reported in only 75 of nearly 400 patients in whom a gastroscopic diagnosis of chronic gastritis was made; superficial gastritis has not been discussed because the number of cases studied intensively was too limited.

A correlation of symptoms occurring in primary chronic gastritis that differ from those of the typical peptic-ulcer syndrome has already been given. These symptoms are merely suggestive, not diagnostic, of the presence of chronic gastritis. Furthermore, gastric analyses showed nothing of positive diagnostic significance regarding either the presence of gastritis or the differentiation of the two types. In addition, x-ray studies were often of inconsequential value in diagnosing the presence of gastritis. Thus, the only dependable method of diagnosing chronic gastritis or differentiating its various types is afforded by gastroscopy.

The symptomatology of chronic primary gastritis usually resembles that of peptic ulcer. However, it is occasionally suggestive of cholecystitis, and more rarely of carcinoma. In the differential diagnosis, one should consider not only these entities but also all others that may cause upper abdominal digestive symptoms, and when hematemesis has occurred, all its causes should be kept in mind. Having thus established gastroscopically the presence of gastritis, one can decide whether it is primary or secondary only by clinical means. Also, what role the gastritis plays in the production of the symptomatology can be decided only by proper clinical interpretation.

A factor useful in differential diagnosis is furnished by the findings in the 10 patients whose symptoms were typical of peptic ulcer. The differential feature is the failure to find x-ray evidence of peptic ulcer, gall-bladder disease or any other cause for the symptomatology. This is a diagnostic feature stressed by Rivers and Smith.<sup>17</sup> Fatigability apparently affords another diagnostic feature since, as emphasized by Schindler and his associates,<sup>15</sup> it is a symptom of atrophic gastritis, and since it was not observed in any case of the hypertrophic type.

Hematemesis resulting from gastritis and occurring in the absence of peptic ulcer, carcinoma, polyp, varicose veins or blood dyscrasias was observed in 3 cases of hypertrophic and 2 of atrophic

gastritis; it was caused by an ulcerating type of gastritis—that is, many superficial ulcerations and fissures were scattered throughout the mucosa. The bleeding varied from mild to severe, but was not fatal.

To study the effect of chronic gastritis on the symptomatology of peptic ulcer, 21 cases of the latter disease were investigated. In only 4 of these were the symptoms apparently modified by the presence of the gastritis, the modification consisting of anorexia or absence of relief of pain by food. Thus, these symptoms, when peptic ulcer is known to exist, suggest the presence of gastritis. On the other hand, their absence does not exclude gastritis.

The tabulations already presented show that the age incidence and chronicity of the hypertrophic and atrophic types of gastritis are comparable. The findings in relation to age incidence confirm those in 21 cases of hypertrophic and 59 cases of atrophic gastritis collected from the literature.<sup>7, 9, 23, 25, 26</sup>

### SUMMARY

The symptomatology of gastroscopically demonstrated primary chronic gastritis was studied and analyzed. Certain symptoms were found to suggest the presence of chronic gastritis.

Hematemesis was an important complication of primary chronic gastritis.

Fatigability was a symptom characterizing primary atrophic gastritis.

The age incidence and the chronicity of hypertrophic and atrophic gastritis were comparable.

The presence of chronic gastritis can apparently be demonstrated only by means of gastroscopy. Nevertheless, the diagnostic significance of the gastroscopic findings must be governed by clinical interpretation.

The incidence of chronic gastritis among our patients was 44 per cent, and there was an approximately even division of the secondary and primary forms. It is estimated that the incidence of primary chronic gastritis among the general population is about 3 per cent.

The symptomatology of peptic ulcer was occasionally slightly modified by the presence of a demonstrable gastritis.

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## MEDICAL PROGRESS

### RECENT DEVELOPMENTS IN AVIATION MEDICINE\*

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UNDER the stimulus of the present emergency, many laboratories in this country and abroad are investigating physiologic problems encountered in high-altitude combat flying. Despite military restrictions imposed by war, the literature of aviation medicine has grown continuously, and the National Research Council has recently authorized the compilation and publication of a classified bibliography of aviation medicine, which will presently be published as a supplementary number of the *Journal of Aviation Medicine*. The following review summarizes material issued within the past two years.

The performance of modern military aircraft taxes the physiologic limitations of the pilot in many ways, and although vast sums have been spent by the Government in the design of aircraft, little so far has been appropriated for study of the

physiologic limitations and protection of the pilot; this lack continues, despite the fact that in Germany some twenty independent laboratories of aviation medicine are supported by the government. The war in the air has come to be in a very real sense a physiologic war, since the limitations of air combat at the present time lie more with the pilot than with the plane, and the government that succeeds in adequately protecting the pilot through study of his physiologic needs will gain strategic advantage that will undoubtedly be decisive in determining the outcome of the conflict. It is therefore incumbent on all who are actively concerned in the present war to become familiar with the general principles of aviation medicine, especially as they relate to high-altitude combat flying.

The more important advances of the last two years relate to the following: the physiologic effects of acceleration; the use of oxygen at high altitudes; air embolism and its prevention; and anoxia of the adrenal glands. The topics are considered in this order; problems of pilot selection and training are not touched on.

#### PHYSIOLOGIC EFFECTS OF ACCELERATION

It is well known that modern combat flying, especially the dive bombing maneuver, causes the development along the longitudinal axis of the body of centrifugal forces that tend to draw blood

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In England the Flying Personnel Research Committee has directed research for the Royal Air Force in Canada a similar committee has been set up since the beginning of the war and in the United States the National Research Council at the request of the armed services formed the Committee on Aviation Medicine in October, 1940. These three committees along with the air corps which they serve are responsible for the principal direction of research endeavor in aviation physiology in the allied countries. These committees have thought fit to publish some of their newer disclosures but other data having strategic military significance cannot be made public at the present time, and hence a review of the subject is to this extent restricted by the exigencies of war. General principles can be discussed but specific details of equipment must necessarily be left for the future.

away from the head, and so to induce a state of collapse from acute anoxia of the brain. The ultimate effect of a given acceleration depends on four factors: the magnitude, the duration, the direction of acceleration, and the physiologic condition of the pilot at the time the acceleration develops. An excellent discussion of the underlying physical principles is found in a recently published volume by Grow and Armstrong,<sup>1</sup> and in a work by Phillips and Sheard.<sup>2</sup> The recent German literature, with a surprising amount of experimental detail, is given by Ruff and Strughold.<sup>3</sup> Data from English sources are summarized by Livingston<sup>4</sup> and Whittingham.<sup>5</sup> All authorities agree that a healthy young adult can withstand a positive acceleration acting along the vertical axis of the body of 4.5 g (four and a half times the force of gravity) for approximately five seconds. Thereafter, vision becomes dim (the so-called "blackout"), and consciousness may be entirely lost. But from the point of view of safety in aviation, the state of the pilot's co-ordination during the seconds prior to loss of consciousness is vital, for judgment and co-ordination are poor when relative cerebral anoxia exists, irrespective of its cause. When one is flying at a high altitude under conditions of relative anoxia to start with, a small degree of acceleration may cause blackout much earlier than at sea level.

The direction of acceleration is also important, and recent studies indicate that the body withstands accelerations applied along the horizontal axis of the body far more successfully than along the vertical axis. Negative accelerations toward the head are highly dangerous because of exaggeration of the carotid-sinus reflexes. Indeed, the average young adult can seldom withstand more than 3 g of negative acceleration for five seconds without "seeing red" and having retinal hemorrhages. This accounts for the fact that stunt fliers are loath to indulge in any form of acceleration when flying upside down.

The condition of the organism has much to do with the capacity to withstand acceleration. All test pilots insist that an alcoholic spree of an evening considerably diminishes tolerance for positive acceleration the next day. More significant than this, however, is the fact, recently emphasized in the German literature,<sup>3</sup> that tolerance is seriously lowered by an empty stomach, and all German fliers are urged before going on dive-bombing maneuvers to have a full meal. The effect of food is explained by the Germans as being probably due to the filling of the visceral blood vessels—because they are filled, further

blood is not readily forced into them by centrifugal action. Blood chemistry is not discussed.

In the recent German literature, the following factors, in addition to the full stomach, are mentioned as favoring the pilot's capacity to withstand acceleration:

*Carbon dioxide.* The inhalation of 5 or 6 percent carbon dioxide, through augmenting the cerebral circulation, increases resistance to acceleration by 1 to 2 g.

*Vasoconstrictor drugs.* Any pharmacologic agent that increases the tone of the capillary wall improves one's ability to withstand acceleration. Pituitrin, adrenalin and adrenocortical hormone have all been mentioned in this connection, but precise data concerning them are not available.

*Pneumatic belts.* Mechanical constriction of the abdomen and of the lower extremities has also been proposed in both the German and English literature to minimize the rush of blood from the head to the visceral bed and the lower extremities. Of these mechanical devices, pneumatic belts and pneumatic trousers have been the devices usually discussed. The Germans state that a pneumatic belt may increase tolerance by 1.0 to 1.5 g, but no one of the present belligerent countries has permitted publication of detailed reports concerning these devices.

*Water suits.* The Germans have also reported on a water suit designed for the prevention of blackout, and although they claim that it notably improves resistance to positive acceleration they state that it is unsatisfactory for other reasons.\*

*Posture.* In a recent paper by Ruff,<sup>6</sup> the problem of posture in relation to acceleration was discussed. The Germans, it appears, favor crouching posture, with flexion of the legs against the abdomen, as one particularly suitable for protection of the pilot against acceleration. If the pilot lies supine or prone at the end of a dive-bombing maneuver, he is also less subject to negative accelerations, but in these postures he is unable to see out or to maneuver his plane without special redesigning of the cockpit and the cockpit controls.

The problem has been studied in this country by Armstrong and Heim,<sup>7</sup> and the physiologic

\*To quote Grow and Armstrong<sup>1</sup>: "The water suit is a closely fitting water-proof garment which is worn next to the skin. What little space is left in the suit after it is put on is filled with water or other suitable fluid. This causes the flier to 'float' in the suit, and during acceleration the water presses on the body equally in all directions. As a consequence the normal effects of acceleration are replaced by a uniform compression of the body which, it is estimated, could be tolerated without difficulty up to 15 g or more."

changes accompanying positive acceleration are admirably summarized by Poppen<sup>8</sup> as follows

Our findings confirm those of Armstrong and Heim. It is scientifically interesting that by these two methods of approach the findings were practically identical. Dr. Drinker and I found the following chain of physiological events incident to high positive accelerations: (i) A drop in carotid pressure is a result of the hydrostatic, centrifugal action on the arterial column. (ii) A drop in jugular pressure incident to the same action upon the venous column. (iii) The centrifugal effect upon the venous column is sufficient to reduce the volume of blood reaching the right auricle. This results in a reduced per beat and per minute output of the heart. This causes a secondary drop in carotid pressure superimposed upon direct arterial effect. (iv) The combined effects reduce the carotid systolic pressure, under moderate accelerations, from an average of 130 mm. of mercury to between 60 and 70 mm. (In one case under 6 g, the pressure dropped to 16 mm.) (v) The reduced pressure causes a profound slowing of the circulation through the brain. (vi) A transient local cerebral anoxemia results. This is adequate to explain the symptoms of high acceleration.

We found further that the drop in carotid pressure was proportional to the acceleration. It increases on successive accelerations at frequent intervals. If the acceleration is discontinued before the secondary reduced heart output, the drop in carotid pressure is insufficient to cause severe anoxemia. This explains the statement often made by test pilots that they would prefer 10 g for 15 seconds to 5 g for 3 seconds.

It should be noted that all factors tending to improve the body's resistance to positive acceleration are those that tend to keep blood in the head. Hence it may be concluded that the phenomenon of blackout and loss of consciousness, which may occur within five seconds of the beginning of the acceleration, is probably due solely to acute anoxia and cannot be attributed to any direct effect of acceleration per se on the cortical neurons.

#### USE OF OXYGEN AT HIGH ALTITUDES

It has long been recognized that oxygen is essential for operations at high altitudes, but the reluctance of the older pilots to use it and the conservatism of the commercial air lines in supplying oxygen to passengers have tended to distract attention from the need for oxygen in the lower altitude ranges. Recently, however, there has been a change of emphasis concerning the use of oxygen, there have likewise been improvements in modes of administration of oxygen and also in supply. A general discussion of the effects of anoxia on the heart and other organs has recently been given by Hoff<sup>9</sup> and also by Gemmill.<sup>10</sup>

*Need for oxygen at the lower altitude ranges.* The studies of McFarland,<sup>11</sup> Barach,<sup>12</sup> and many observers in Europe have indicated that mental functions are gravely impaired when human beings are exposed to an oxygen partial pressure equivalent to that encountered at an altitude of 12,000 feet. Thus, when a series of Barach's stu-

dents breathed 13 per cent oxygen over a period of three hours, conspicuous emotional changes developed that were characterized at first by overconfidence, elation and ideational fixations and after an hour or so passed over into a feeling of dullness, lethargy, headache and lack of emotional restraint. Experienced pilots flying without oxygen at 12,000 feet have frequently given testimony of similar strain, irritability, discomfort and bad judgment.

If such grave changes are manifest at 12,000 feet, one naturally wishes to know what other functions may be impaired at the same time, and how soon in the course of ascent the changes can be recognized. Little by little, evidence is accumulating that vision, especially night vision,<sup>14, 15</sup> becomes conspicuously impaired. The gunner begins to lose accuracy of aim even at 8000 feet, the reaction time of the pilot in response to radio signals, or in facing danger in combat, is increased between 5000 and 10,000 feet, varying markedly with individual fliers.

In the cardiac sphere, White<sup>16</sup> reports on electrocardiograms taken on 45 supposedly normal persons exposed to altitudes as high as 20,000 feet with varying rates of ascent (see also Hoff<sup>9</sup>). The changes in the electrocardiogram, especially in the T wave, were noted in all subjects at about 5000 feet, the changes being conspicuous if the rates of ascent were rapid. U waves also became prominent with increasing anoxia, and since all changes disappeared on administration of oxygen, White concludes that myocardial anoxia is the cause of the alterations. As a result of his studies, White recommends that, to secure physiologic normality in a pilot, oxygen should be taken at altitudes above 5000 feet and that it should be mandatory in any flight exceeding 7500 feet. Similar changes in the electrocardiogram of animals have recently been observed by Wiggers<sup>17</sup> and in unpublished studies in this laboratory.

The use of oxygen in the lower altitude ranges has also become an established practice among high altitude squadrons for the sake of washing out nitrogen, which in the higher altitude ranges is likely to give rise to 'bends'. Benson<sup>18</sup> finds that in normal subjects there is no change in the electrocardiogram if pure oxygen is breathed up to 30,000 feet.

*Oxygen mask.* Oxygen masks have been the subject of much discussion and study since the outbreak of the war. The BLB mask was the only one commercially available in the United States at the beginning of the present war, and the old pipestem method of administering oxygen was still in use. The pipestem has proved dangerous and difficult for high altitude operations, because it prevents the pilot from speaking and

is likely to drop from his mouth in the event of a serious emergency. All opinion, therefore, is in essential agreement that a face mask must be used for oxygen administration.

The original B.L.B. mask, both the nasal and the auronasal, had, for pilots, disadvantages that do not apply to patients lying prone in bed, for whom the masks were originally devised. One of the most serious difficulties was that at higher altitudes the valves of the mask tended to freeze, and the mask itself tended also to freeze to the face and thus irritate the skin.

Many special masks have lately been proposed with a view to obviating these difficulties. Thus, Barach and Eckman<sup>19</sup> describe an improved nasal mask. Other masks are now undergoing service tests in this country and abroad, and it is hoped that one will be found answering the ideal specifications recently set forth by Poppen,<sup>20</sup> namely, that the mask must be comfortable to wear, that it must have provision for microphone communication, that its valves must not freeze at  $-50^{\circ}\text{C}.$ , and that some provision must be made to vary the supply of oxygen in accordance with the respiratory needs of the pilot as these change. The actual details of how these requirements are being met cannot be discussed here.

**Oxygen supply.** Oxygen tanks remain the chief source of supply in all combat ships. In large bombers having a personnel of eight or ten during flight, in which missions are long and the altitude high, the oxygen tanks add very considerably to the weight load, and hence various proposals have been made to manufacture oxygen in flight. It is not a military secret that no one of the proposals for separating oxygen in the air has so far proved satisfactory. The new aluminum alloy tanks, however, have very considerably diminished the weight load, but since they are more vulnerable to machine-gun penetration they probably form a greater hazard to the pilot and the ship than the older, heavier oxygen tanks.

Pressure-cabin planes have so far not proved feasible for light combat craft.

#### AIR EMBOLISM AND ITS PREVENTION

During the course of the present war, certain pilots in high-altitude squadrons have experienced grave symptoms that could not be attributed to anoxia, acceleration or any form of metabolic disturbance. Susceptible persons, some at altitudes as low as 25,000 feet, developed paresthesias, with numbness and itching, sometimes restricted to the face, but often occurring sporadically all over the body. Later, aches and a sense of deep localized pressure often developed in one or more of the peripheral joints, especially the knuckles and wrists and occasionally also in other joints, particularly

if there had been previous injury. These premonitory symptoms are followed sometimes quite quickly by the development of intolerable deep pain variously described as rheumatic or like that of a toothache, and often referred to a given joint or to a previously injured long bone—one of the best recent descriptions of this type of pain is that of Streltsov,<sup>21</sup> of the Pavlov Laboratories in Moscow. These intense deep pains are indistinguishable from those experienced by divers in the familiar syndrome of the "bends."<sup>22</sup> Recently, diving crews familiar with the bends have been subjected to decompression, and they have experienced at altitudes equivalent to 28,000 and 35,000 feet symptoms closely parallel with those which they had had when emerging too rapidly from an undersea dive.<sup>23</sup> Severe bends may be followed by collapse, pallor, sweating and respiratory difficulty all developing with catastrophic rapidity. Such collapse has been thought to be due to sudden pulmonary air embolism.

Proof that high-altitude bends are caused by the liberation of nitrogen has been somewhat difficult to establish by direct observation, but the indirect evidence of similarity of symptoms is highly impressive (see Armstrong<sup>24</sup>). Quite recently, Walsh and Boothby<sup>25</sup> have found that bubbles begin to appear in the cerebrospinal fluid of human beings in a decompression chamber when subjected to a pressure equivalent to an altitude of 12,000 feet. The bubbles were fine, like those rising in good champagne. They became larger and more numerous at pressures approximating those of 28,000 feet, but after ten minutes' exposure to such altitudes the bubbles decreased in number and size, and later disappeared. The cerebrospinal-fluid pressure in these circumstances rose to a level 3 cm. higher than normal. This was believed to be due to the expansion of air bubbles.<sup>26</sup>

If bends occur as commonly as one might be led to suppose from the early reports, especially from observations made on men of older age groups, this condition is clearly a serious hazard for fliers. However, it has been found by Armstrong<sup>24</sup> and by many others who have lately investigated the problem that there is a large individual variation in susceptibility and that bends occur less commonly in the younger age group, for example, from eighteen to twenty-four, the average age of the combat flier, than in the older age group. Decompression-chamber tests suggest, moreover, that at least 50 per cent of a population of young male adults can withstand altitudes as high as 40,000 feet for periods of from one to six hours without developing bends. Hence it has been suggested that the high-altitude squad-

rons be selected on the basis of decompression-chamber tests

Since bends are undoubtedly due to the formation of nitrogen bubbles in the tissues, an obvious suggestion would be to rid the tissues of their nitrogen by replacing the latter with helium<sup>21</sup> or by preoxygenation. This proposal has been studied by Behnke<sup>8</sup> and others. Armstrong and Heim,<sup>9</sup> for example, find that inhalation of pure oxygen from half to one hour before ascent prevents bends. But Whittingham,<sup>40</sup> in reviewing Armstrong and Heim's paper, mentions that observations in England have shown that inhalation of oxygen merely delays the onset of bends and does not actually prevent it. Furthermore, the recently published curves of Behnke and Willmon<sup>22</sup> indicate that at least five hours are required to eliminate nitrogen from the body by oxygen inhalation, and that owing to the fatty deposits in the marrow of the long bones, the bone marrow tends to hold its nitrogen more firmly than other tissues do. Since some at least of the deep pain associated with bends probably arises from bubble formation in the long bones, it would be essential to have at least five hours of preoxygenation to give a subject complete immunity from the distressing syndrome.

It is obvious, therefore, that from the point of view of combat flying it is not feasible to protect a flier by causing him to breathe oxygen for five hours before going up. But with careful selection of personnel for high altitude operation, and with the delaying effects of pure oxygen from the ground up, bends cease to be a serious problem in military aviation.

Likewise for practical reasons, the use of helium to replace nitrogen has not been found feasible for combat pilots.

#### ANOXIA OF THE ADRENAL GLANDS<sup>31</sup>

In a little quoted paper by Kellaway,<sup>32</sup> published in 1919, it was pointed out that a cat subjected for several hours to low-oxygen tension exhibits a rise of blood sugar and an increase of heart rate, both of which the author attributed to active secretion of the adrenal medulla during decompression, paradoxical dilatation of the denervated pupil occurred, a phenomenon that had already been proved to be due to the liberation of adrenaline, since section of the splanchnic nerves completely abolished the dilatation. When the splanchnic nerves were sectioned, the blood-sugar elevation was abolished initially, but Kellaway encountered several animals, not fully accounted for in his protocols, in which after more prolonged exposure, the blood sugar actually rose.

Kellaway was not aware of the significance

of the adrenal cortex, and it remained for Evans,<sup>33</sup> fifteen years later, to elucidate its action.\* The latter observed a striking increase in the glycogen content of the liver and in the glucose level of the blood of rats exposed to half an atmosphere pressure in a decompression chamber, and he proved that the phenomenon failed to occur after adrenalectomy. He did not cut the splanchnic nerves, but he found that adrenocortical hormone restored the blood sugar and glycogen response in a specific manner. When exposed for twenty-four hours to the rarefied atmosphere, containing 10.5 per cent oxygen, the glycogen content of the liver of a normal animal increased ten to twenty times above its resting level, and the blood glucose increased markedly. Since the total carbohydrates in the animal had become augmented, it was evident that glucose must be formed from noncarbohydrate sources, probably entirely from proteins.

These observations have more recently been confirmed by a number of investigators, notably by Long et al.<sup>34</sup> and by Thorn and his collaborators.<sup>37</sup> Armstrong and Heim<sup>28</sup> found that hypertrophy of the adrenal glands occurs when animals are exposed repeatedly to low partial pressures of oxygen, suggesting that some substance is elaborated in the adrenal cortex when an animal is adjusting to anoxia. Strong confirmatory evidence pointing in this direction came in 1937 from Giragossintz and Sundstroem,<sup>39</sup> who pointed out that it took ten times as much adrenocortical extract to maintain adrenalectomized rats at half an atmosphere as it did at sea level. Very little clinical evidence is as yet available concerning the behavior of the adrenal cortex in man exposed to high altitudes, and it is not yet clear whether the administration of adrenocortical hormone in man facilitates his adjustment to high altitude or improves his performance. The results recently reported by Kendall<sup>40</sup> suggest that the corticosterone fraction rather than the desoxycorticosterone is responsible for the carbohydrate changes and possibly, therefore, for the adjustment to altitude. Armstrong<sup>23</sup> has suggested that the physical collapse which occurs in combat pilots after excessive exposure to diminished oxygen pressure may be due to atrophy of the overworked adrenal glands, the syndrome being essentially similar to that of Addison's disease. Huddleson and McFarland<sup>41</sup> have found that the administration of adrenocortical hormone is beneficial in cases of psychasthenia.

\*Observations bearing on the reaction of the adrenal glands in anoxia, but in which no clear distinction is made between the adrenal cortex and the adrenal medulla, are found in the papers of Binet and Labrosse<sup>42</sup> and Housay and Rietti.<sup>43</sup>

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CASE RECORDS OF THE  
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

## CASE 27331

## PRESENTATION OF CASE

*First Admission.* A thirty-eight-year-old, Irish-born, single domestic was admitted to the hospital complaining of joint pains.

Two and a half years before admission, the patient began to suffer from attacks of arthritis characterized by redness, heat, swelling and limitation of motion in the various joints. Her feet, shoulders and sternoclavicular joints were first involved, and later her knees and the small joints of the fingers and hands. These attacks lasted for long periods, and to control the pain she took Oxyliodide, a proprietary drug containing cinchophen.

One year before admission, the patient became progressively more tired and noticed an increasing jaundice of the skin, without pruritus. Vomiting ensued, the stools became pale, and drowsiness was so pronounced that she slept most of the time. Abdominal distention developed, and a paracentesis was performed on three occasions. Severe nosebleeds occurred, and at the time of admission the patient had lost 20 pounds. She was in another hospital the best part of three months, and during this time the joint pains were in abeyance. Her strength and appetite gradually returned, and the jaundice faded; five months before entry, however, the joint pains returned.

The family history was irrelevant. Seven years before admission, the patient had had "jaundice," for which she was treated in another hospital. Nosebleeds had occurred for several months before the onset of her illness two and a half years previously.

Examination showed a poorly nourished, slightly jaundiced woman with minimal generalized adenopathy. There were signs of fluid at the right base. The heart was not enlarged, but a systolic murmur was audible; the blood pressure was 150 systolic, 80 diastolic. The abdomen was protuberant, with shifting dullness, and a small umbilical hernia was noted. The liver was palpable two fingerbreadths below the costal border, and the spleen was easily felt. The fingers were tapering and spindled; the ankles, elbows and knee joints were swollen, tender and limited in motion.

The temperature, pulse and respirations were normal.

The urine was normal. The stools were guaiac positive on one occasion but negative on six other examinations. Examination of the blood showed a red-cell count of 3,360,000 with 60 per cent hemoglobin, and a white-cell count ranging from 3400 to 6400, with a normal differential. The blood film showed moderate hypochromia, anisocytosis and poikilocytosis. The blood Hinton reaction was negative. The blood nonprotein nitrogen and uric acid were normal. The serum protein was 4.7 gm. per 100 cc. The serum van den Bergh was normal indirect, and the icteric index 4. The Takata-Ara test was strongly positive, and the bromsulphalein excretion showed 10 per cent retention of the dye. The blood sedimentation rate was 0.43 mm. per minute. Gastric analysis showed no free fasting acid but did show 10 units after histamine; a guaiac test was positive. A sugar-tolerance test was normal, the fasting value being 85 mg. per 100 cc. The basal metabolic rate was +19 per cent. An electrocardiogram showed slight left-axis deviation.

X-ray films of the involved joints showed narrowing of the joint space, irregularity of the articular surface, new-bone formation about the margins and marked decalcification. The Graham test showed the presence of a small stone within a poorly functioning gall bladder. Examination of the colon, sinuses and jaws was negative save for a single incisor-root abscess. A film of the chest showed a high right diaphragm, a slightly dull right cardiophrenic angle and a slight shift of the heart to the right.

During a three months' stay in the hospital, the patient's oral temperature frequently reached 100°F. On one occasion, she was given 3 gr. of Nembutal and ¼ gr. of morphine, with the result that she slept for three days and her temperature rose to 102°F. The patient was maintained on a regimen of high vitamins and physiotherapy, but responded so poorly that she was discharged to a hospital for chronic patients. On one occasion, an abdominal paracentesis yielded 6500 cc. of light-yellow fluid.

*Final Admission* (five years later). During the intervening five years, the joint symptoms and disability did not progress, but the patient had slight recurrent ascites and jaundice from time to time. She was readmitted complaining of nonradiating subxiphoid postprandial pain, usually followed by nonprojectile vomiting and unrelieved by food or milk. For two weeks, she had been unable to keep anything down, even water. The vomitus was never blood stained, and there was no change in bowel habits, or blood by rectum.

Examination was unchanged, except that the liver edge was no longer palpable (one observer excepted) and that there were no signs of ascites. The blood pressure was 130 systolic, 80 diastolic.

The temperature, pulse and respirations were normal. The urine was normal except for +++ test for bile on one occasion. The blood was normal. The stools were guaiac positive twice in five determinations. The blood chemical findings showed normal vitamin C, uric acid, protein and bilirubin levels; bromsulfalein excretion was normal. The prothrombin time was 33 seconds, the normal being 20 seconds. The corrected sedimentation rate was 0.3 mm. per minute. The Congo red test showed 50 per cent remaining in the blood at one hour. Gastric analysis showed no free acid. An electrocardiogram showed, as before, a moderate left-axis deviation.

X-ray films of the joints showed progression in the pathologic process and considerable bone atrophy, especially of the shoulder girdle. Examination of the gastrointestinal tract was suggestive of esophageal varices and demonstrated a 2.5-cm. by 1.0-cm. ulcer crater in the antrum, the center of the crater lying 3.5 cm. proximal to the pylorus. The appearance was that of a benign ulcer.

The patient was started on an ulcer regime and physiotherapy. The prothrombin time having risen to 55 seconds, she was given synthetic vitamin K, with a return to 31 seconds. The gastric symptoms disappeared, but a film taken two weeks after the first showed no diminution in the size of the ulcer.

One month after admission, the patient developed photophobia, with conjunctival injection, and corneal ulcers were noted, so that she was transferred to another hospital for further care. After a week's stay, during which the keratitis did not improve, being ascribed to riboflavin deficiency, her temperature rose suddenly to 101°F., and she became slightly disorientated and incoherent. The following day, the temperature was 102°F., and she was transferred back to the medical service of this hospital.

Examination showed an acutely ill woman lying flat in bed, with labored respirations, slight cyanosis of the lips and a dry tongue. The heart and lungs were unchanged. The blood pressure was 100 systolic, 60 diastolic. The abdomen was markedly swollen, and there was sagging in the flanks. Spasm was present throughout, and compression of the umbilical hernia produced a tinkling, gurgling sound. Peristalsis was absent. The patient expired a few minutes after examination.

## DIFFERENTIAL DIAGNOSIS

DR. ALFRED O. LUDWIG: In this case, we are dealing with a woman who obviously had chronic progressive rheumatoid arthritis and several complications that might go with that disease or with its treatment. The first important statement in this history is that she took a drug containing cinchophen. It is quite well known that cinchophen occasionally produces subacute or acute yellow atrophy of the liver. Although such sensitivity is infrequent, it is important to recall that of 190 cases reported up to 1933, 46 per cent were fatal. It is probable that many cases are unreported, so that the incidence of toxicity may be much more frequent. Because of the serious nature of such reactions, we no longer use the drug in this hospital. One should remember that, as in this case, toxicity may not develop until several months after the taking of the drug, and that it may also occur with small doses, one case being reported following a single dose of 7.5 gr. This woman developed the typical clinical picture of subacute yellow atrophy, with drowsiness, ascites, jaundice and an increased bleeding tendency. During the time she was jaundiced, she apparently had a remission of the joint symptoms. This phenomenon has been previously reported, particularly by Hench\* of the Mayo Clinic, who points out that the quantity, not the quality, of the jaundice, is important. He states that a blood bilirubin level of 8 mg. or more per 100 cc. is necessary before much improvement in joint pain occurs. Such remissions may last anywhere from five weeks to one and a half years; then usually, as in this case, the joint pain returns. It is of further interest that this patient had jaundice seven years before admission and some four years before she began to take cinchophen. There is some evidence that cinchophen may be more toxic to patients who have had previous liver damage, regardless of cause.

Examination showed a slight generalized adenopathy that might very well have been a part of the rheumatoid arthritis. Adenopathy is not infrequent in rheumatoid arthritis and may also be associated with splenomegaly. I believe the fluid at the right base was secondary to the acute disturbance in the liver. It is quite common in such cases, and is probably due to irritation of the pleura over the diseased organ. The patient obviously had ascites, again secondary to the liver disease. The

\*Hench, P. S., Bauer, W., Dawson, M. H., Hall, F., Holbrook, W. P., Key, J. A., and McEwen, C. The problem of "rheumatism" and arthritis: review of American and English literature for 1938. *Ann. Int. Med.* 13:1837, 1939, 1940.

enlarged spleen was undoubtedly associated with the hepatitis rather than with the arthritis. The examination of the joints is characteristic of rheumatoid arthritis. The guaiac-positive stools are related to an increased bleeding tendency from liver disease. That is also true of her anemia and leukopenia. A lowered serum protein is quite frequently associated with liver disease, although it may also be found in long-standing cases of rheumatoid arthritis. At the time she arrived at the hospital, the acute process in the liver had subsided considerably, because the van den Bergh was normal, and the icteric index only 4. A positive Takata-Ara test confirmed the diagnosis of liver disease. This test depends on the presence of an increased amount of globulin in the blood. It is usually positive only with a severe degree of liver disease. The bromsulfalein test showed 10 per cent retention, which is also consistent with the diagnosis of liver disease. The sedimentation rate was just at the upper level of normal by our method. The patient had a somewhat low fasting sugar value, which again may be related to the liver disturbance.

I think it might be worth while to see the x-ray films.

DR. TRACY B. MALLORY: There is no x-ray man here, unfortunately.

DR. LUDWIG: In the absence of expert opinion, I shall have to limit myself to the findings in the joints. I should like to have some help in determining the character of the lesion in the stomach.

The joint findings are characteristic of chronic rheumatoid arthritis. The irregularity and narrowing of the joint spaces and the marked atrophy of the bones, with evidence of joint destruction and subchondral cysts are consistent with rheumatoid arthritis.

There were several examinations for esophageal varices, and I gather that they were thought to be present.

DR. MALLORY: Dr. Aubrey O. Hampton, on interpreting the films, thought they probably were present but could not be certain.

DR. LUDWIG: I am led to believe that they thought the ulcer was benign. Is that correct?

DR. MALLORY: It is, so far as the fluoroscopic findings and films are concerned.

DR. LUDWIG: Her marked overreaction to Nembutal and morphine is also of diagnostic value. We have observed such sensitivity to morphine in a number of patients with proved hepatic cirrhosis. In such cases, even small amounts of morphine may cause death.

The diagnostic problem here is to decide what caused death. From the history, I think we must

conclude that this patient did have toxic cirrhosis of the liver, almost certainly secondary to the ingestion of cinchophen. However, the symptoms before her last admission seem to have been due to the presence of a gastric ulcer. The laboratory examination showed an increased prothrombin time, which is consistent with the liver damage. It is of some importance that the gastric analysis showed no free acid whatever at that time. This is unusual but not unheard of with benign gastric ulcers. It may be significant that the liver decreased in size over five years.

The Congo red test showed 50 per cent retention in the blood, and the test was probably carried out as part of an investigation of the incidence of amyloidosis in rheumatoid arthritis. This complication may occur as part of the disease, usually in chronic cases of long duration or in children with the severe Still's type. A loss of 20 to 30 per cent from the blood in one hour may be considered normal. Here, the loss of 50 per cent may be significant and may mean that this patient had a degree of amyloidosis. I do not believe that the eye lesions were secondary to the rheumatoid arthritis, although iritis occurs in 5 per cent of the cases in some series. Scleromalacia perforans is occasionally seen with rheumatoid arthritis and is thought to be due to the formation of rheumatic nodules on the sclera. It is possible that vitamin deficiency played a part in this case, owing to an inability to absorb these substances normally.

The final episode is poorly described. I cannot escape the conclusion that this patient died of general peritonitis. If that is so, perforation of the ulcer would be the most likely cause; however, one would expect some history of pain. At the time she re-entered this hospital, she obviously had fluid in the abdomen. The statement that there was a tinkling sound on compression of the hernia may mean that there was also free gas in the peritoneal cavity. This would be further evidence that a viscus had perforated, in this case the stomach. The ulcer may have been malignant. The absence of free acid is slight confirmatory evidence of malignancy, and the fact that the ulcer did not decrease in size over a period of two weeks is additional evidence. I do not know how we can decide that question other than by microscopic examination. Gastroscopy apparently was not done.

Are there any other conditions that should be considered? One might think of acute hepatic failure, but I do not believe the evidence given here allows such a diagnosis. The patient did not become jaundiced again, and there are none of the other characteristic findings of acute hepatic

failure. One wonders, with the previous history of stone in the gall bladder, whether she might have had an acute cholecystitis with perforation of the gall bladder; but again the evidence does not allow us to conclude this. If a gallstone played any part, she might also have had acute pancreatitis, but again the evidence is lacking. I shall make diagnoses of chronic rheumatoid arthritis, toxic hepatic cirrhosis and an acute perforation of a gastric ulcer, with general peritonitis. Microscopically, there may be some degree of amyloid disease as well.

DR. CHARLES L. SHORT: I saw this patient several times, and I think she was once a living example, and is now a dead example, of the dangers of cinchophen—the United States Food and Drug Administration has taken recognition of the dangers of cinchophen and aminophyllin and has placed certain restrictions on their use. She was disabled for the remainder of her life following cinchophen intoxication. The fact that she developed an ulcer is of some theoretical interest because acute gastric ulcers can be readily produced in dogs that have been given toxic doses of cinchophen. In fact, it is much easier to produce an ulcer in dogs after cinchophen than it is to produce liver damage. Whether her ulcer had any relation to cinchophen is quite doubtful. I do not know of any other cases in man that have been reported.

DR. WYMAN RICHARDSON: Is it true that in your material here the incidence of ulcer and liver disease is a commoner combination than that due to chance?

DR. MALLORY: I cannot say that it is. I thought for a time that it was, but as we see more cases, such a combination does not come up very frequently.

#### CLINICAL DIAGNOSES

Gastric ulcer.  
Cirrhosis of the liver.  
Rheumatoid arthritis.

#### DR. LUDWIG'S DIAGNOSES

Rheumatoid arthritis, chronic.  
Toxic cirrhosis of the liver.  
Gastric ulcer, with perforation.  
General peritonitis.

#### ANATOMICAL DIAGNOSES

Chronic rheumatoid arthritis.  
Toxic cirrhosis of the liver (probably due to cinchophen).  
Benign peptic ulcer, with perforation.

General peritonitis.  
Pneumoperitoneum.  
Splenomegaly.  
Esophageal varices.

#### PATHOLOGICAL DISCUSSION

DR. MALLORY: Dr. Ludwig has made this very complicated case seem almost absurdly easy. The patient showed an extremely small liver, weighed only 650 gm., which was also the weight of the greatly hypertrophied spleen. Esophageal varices were present and very readily demonstrated at autopsy. There was no evidence, however, that they had bled at any recent period. There was a large ulcer in the stomach just at the edge of the prepyloric area. It measured 3 cm. in length, 1 cm. in width and 1 cm. in depth. We were very suspicious that it might prove to be malignant, and therefore cut a considerable number of microscopic sections through its margin, all of which showed a perfectly benign mucosa. We must accept it as a benign ulcer in spite of the fact that this patient showed so very little hydrochloric acid in the gastric secretions. The test was positive on only one occasion, and then weak. The final episode was a perforation of the gastric ulcer, and there was generalized peritonitis, with considerable amounts of air beneath the diaphragm, which showed up clearly on post-mortem x-ray plates. There were, of course, all the usual changes of a severe chronic rheumatoid arthritis.

A PHYSICIAN: Was there any amyloid disease?  
DR. MALLORY: No.

#### CASE 27332

##### PRESENTATION OF CASE

A thirty-four-year-old woman entered the hospital complaining of the sensation of a lump in her throat.

The patient felt well until two years before admission, when the sensation of a lump in the throat appeared just above the suprasternal notch. It was constant, felt like "a piece of apple" in the throat, and was aggravated by swallowing, although there was no difficulty in swallowing or in breathing. The symptom disappeared within three weeks but returned from time to time when the patient was overworked, tired and nervous.

Four months before admission, the sensation once again became constant and grew worse, producing slight difficulty in swallowing if food was taken too quickly. The patient stated, "The morsel seems to stick in my throat for a moment." Two months later, she saw her physician, and at

this time a constant substernal burning sensation had appeared; x-ray films of the chest were taken. Two weeks before admission, the patient stopped work, and immediately her symptoms subsided.

At no time had there been cough, hoarseness, dyspnea or weight loss. For the previous week, the patient had noticed a dull pain on movement of the left elbow, wrist and thumb. She had suffered from diphtheria and the usual childhood diseases. The family history was irrelevant.

On examination the patient was well developed and well nourished and in no apparent discomfort. The thyroid gland was palpable in the suprasternal notch during swallowing. The cardiac apex and left border of dullness were in the anterior axillary line. A blowing systolic murmur was heard at the apex and in the aortic area; the blood pressure was 120 systolic, 85 diastolic. Examination of the lungs, abdomen, pelvis and nervous system was negative.

The temperature, pulse and respirations were normal.

The urine was normal. The blood showed a red-cell count of 5,200,000 with a hemoglobin of 80 per cent, and a white-cell count of 10,600 with 67 per cent polymorphonuclears. A blood Hinton reaction was negative.

An x-ray film of the chest showed a round soft-tissue mass approximately 6 cm. in diameter behind the heart in the angle between the spine and diaphragm on the left side. The esophagus touched its anterior wall, but was probably not adherent to it. The mass did not pulsate and showed no evidence of calcification. The base of the right upper-lung field was unusually bright, the heart was normal in position, and the spine showed no abnormalities in the region of the mass.

Films taken in the upright and horizontal positions, with the patient lying on the right side, failed to show definite change in the size of the mass.

An electrocardiographic recording showed normal rhythm at 90, with a PR interval of 0.14 second. There was a tendency to right-axis deviation. T<sub>2</sub> was low, T<sub>3</sub> slightly inverted.

On the fourth hospital day, an operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR. JACOB LERMAN: The story is that of pressure symptoms in the neck of two years' duration, with a sensation of a lump in the throat, but no hoarseness and no difficulty in breathing. There is no mention of an objective pressure symptom, namely, clearing of the throat, which the patient

usually disregards. The symptoms became worse four months before entry, and in addition, difficulty in swallowing became definite. There is no mention of cough, hoarseness, dyspnea, pain in the chest or cardiac embarrassment. When the patient stopped work, the pressure symptoms subsided. On the whole, pressure symptoms in the neck fluctuate considerably, depending on such factors as nervousness, fatigue and rest.

Physical examination revealed no discomfort, and the patient was able to breathe properly. The thyroid gland was palpable, but no mention is made of its size. The description is that of a substernal gland, because when she swallowed, only the top portion could be felt.

The x-ray report fails to mention the thyroid gland. It seems that if the gland were in the position described, the radiologist should have visualized it, particularly after a swallow of barium. There is no mention of this procedure. According to the x-ray examination, the heart is not displaced by the mass in the posterior mediastinum. We should expect some deformity of the trachea, not only from the mediastinal mass but also from the goiter that was felt in the suprasternal notch. However, there is no description of the trachea.

The electrocardiogram may be unimportant, or may indicate pressure on the heart by the tumor, producing slight right-axis deviation.

The differential diagnosis boils down to some form of mediastinal tumor. The first question I should like to settle, assuming it was neoplastic, is whether it was benign or malignant. It seems from the description that the tumor was not malignant. It is described as a discrete lump, which fits in with a diagnosis of benign tumor. The absence of tissue destruction, as indicated by freedom from pulmonary infection and toxemia, and the absence of venous obstruction, involvement of the recurrent laryngeal nerve or erosion of bone argue against malignancy. Of the benign tumors, one must consider neurofibroma, fibroma, chondroma, myoma, dermoid and simple cyst.

The evidence is against aneurysm. Presumably, the aorta was visualized and found to be distinct from the mass, which did not pulsate; the blood Hinton reaction was negative. One ought to consider a diverticulum of the esophagus, which could produce such a large mass. Certainly, in this event, x-ray study should have revealed a connection between the esophagus and the mass. Also, a large diverticulum would change in appearance with change in position. It occurred to me that a large diaphragmatic hernia could produce this picture. Here, also, the radiologist would have visualized the connection between the mass and

the stomach, and the mass would have changed in size and shape with change in position.

Because of the presence of a goiter, one must consider the possibility that an intrathoracic goiter had moved down from the usual position and had gradually wandered to the bottom of the thoracic cage. Any tumor of thyroid origin that lies below the superior strait has to descend as it grows. If it descends below the level of the arch of the aorta, it can grow laterally or posteriorly. The fact that the symptoms were intermittent suggests that the mass grew intermittently. This is consistent with the growth of a portion of a substernal goiter downward into the posterior mediastinum. I am assuming that the examiner found a substernal thyroid gland. Against this assumption is the lack of pressure symptoms. I should like to know more about the x-ray appearance of the esophagus and trachea.

DR. CHARLES L. SHORT: I saw these x-ray films, and there was no sign of a substernal thyroid gland. I also examined the patient before x-ray examination was made and did not feel any goiter.

DR. LERMAN: The examiner was very explicit. Should I take his findings at their face value or be influenced by what Dr. Short has said? The position of the mass is consistent with intrathoracic goiter. I have seen similar tumors that have "plunged" into the thorax and assumed positions either lateral or posterior to the heart without producing much deformity of the adjacent organs. I shall have to consider, first, a large intrathoracic goiter and, secondly, and commoner, a benign tumor of the mediastinum, such as a neurofibroma. The x-ray report mentioned that the base of the right upper lung was unusually bright. This was probably due to compensatory emphysema of this lobe as a result of partial collapse of the right middle and lower lobes.

DR. SHORT: I saw this patient before she had an x-ray examination, and she certainly gave the appearance and the story of a patient with functional symptoms. I was rather surprised when the x-ray report of mediastinal tumor came back.

There was one interesting thing in the physical examination—the apparent displacement of the heart to the left. I think that might have given us a clue to the presence of tumor in the chest. I should be interested to know whether the heart was actually displaced. The murmur was not enough to make a diagnosis of organic mitral regurgitation. The x-ray films that I saw were even more confusing, because the tumor mass

was first interpreted as being cystic, the most probable diagnosis being a congenital cyst of the lung. On the basis of that and of the patient's story, it seemed unlikely that the mass was causing symptoms. I was rather hesitant about advising operation without having a period of observation, but she had the tumor removed.

DR. LERMAN: There is nothing here to indicate that the heart was displaced. It was normal on x-ray examination.

DR. SHORT: Yes; but on physical examination, the apex was clearly palpable outside the mid-clavicular line.

DR. LERMAN: Did you mean displacement anteriorly?

DR. SHORT: I just said displacement. I suppose it was anterior rather than to the left, but the apex was certainly felt outside the mid-clavicular line, and in the absence of intrinsic heart disease, I should assume that there was some mass in the mediastinum displacing the heart.

DR. EDWARD D. CHURCHILL: This case, like others we have recently discussed, shows the chaotic state of the interpretation of symptoms arising from mediastinal tumors, and is characteristic of those of a very large number of patients. The symptoms seem completely removed from anything that this tumor could possibly have done and so remote, as Dr. Short has intimated, that one might be entirely convinced that they have nothing to do with a mediastinal tumor. I think that is often so. Frequently, as in this case, we have not been at all convinced that the mediastinal tumor has had anything to do with the symptomatology; yet the patients must be treated. There are sensations that do arise from tumor in the mediastinum, and patients not infrequently have great difficulty in finding words to express just what they are experiencing. It is not pain; it is not oppression; it is not covered by the usual words that doctors use to describe sensations. Or we ask them these questions, and they say, "No," but they eventually find a word for it. The result is that I have seen patients with malignant tumors of the mediastinum carried on for long periods as neurotics simply because they could not express what they were experiencing. I think the decision to operate must be based on the frustration and impossibility of knowing what type of tumor one is going to find and what that tumor is going to do for the next few years.

#### CLINICAL DIAGNOSIS

Neurofibroma of mediastinum.

## DR. LERMAN'S DIAGNOSES

Intrathoracic goiter or mediastinal neurofibroma.  
Partial collapse of right middle and lower lobes.

## ANATOMICAL DIAGNOSIS

Neurofibroma of mediastinum.

## PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This patient was explored, and a fibromatous tumor that apparently arose from the sympathetic chain was found. It lay just above the diaphragm and lateral to the aorta. It had pushed the lower lobe forward and had produced partial collapse. Histologically, it was a fibromatous tumor, with some areas of what we call "palisading," which suggest a neurogenous origin. It also showed extensive areas of xanthomatous degeneration, large parts of the tumor being bright yellow. On histologic examination, these yellow areas were composed largely of mono-

nuclear phagocytes containing cholesterol, similar to those found in atheromatous plaques. The diagnosis of neurofibroma is not open to any question.

DR. RALPH ADAMS: This patient was well from the time of operation, two years ago, until last fall. At that time, she was seen because again she had the sensation that a morsel was sticking in her throat, and she complained of nervousness, irritability and difficulty in swallowing. These symptoms had been precipitated by the persuasive arguments of a young man who wished to marry her. X-ray films were negative, and she was reassured about her general condition.

DR. LERMAN: Was there any comment at operation about where the thyroid gland was located?

DR. MALLORY: I do not think they got anywhere near it. The operative incision was low and posterior?

DR. CHURCHILL: Yes; it was well down.

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## PREVENTIVE GERIATRICS

THE paper covering the potentialities of preventive geriatrics that appears in this issue of the *Journal* will have something of an emotional appeal to all but our youngest readers, for it embodies an outlook on advancing years that is generally cherished in middle age. That for which we all fondly hope as we reach the climacteric presents a pleasant prospect and makes good reading, even though we know it cannot be attained by all. That it may become more generally attainable, however, is not entirely a wistful hope but a reasonable, and perhaps even a scientific, goal for which to strive. Just as pediatrics has thrived on the irresistible urge of the baby to grow up, so may geriatrics promote itself by husbanding the natural involutional processes that tend to adjust

and protect the earthly tabernacle against the ravages of time.

It is to be hoped that this promotion will not be forced, as it sometimes has been in political discussions that have moved along parallel lines. Much more knowledge of the physiology of age—here called gerontology—is needed before we can know how to improve our present habits. The conviction that they are not the best possible habits has long been entertained and expressed, as by Lord Rosebery:

It is a black moment when the heralds proclaim the passing of the dead, and the great officers break their staves. But it is sadder still when it is the victim's own voice that announces his decadence, when it is the victim's own hand that breaks the staff in public. I wonder if generations to come will understand the pity of it!

It is to be hoped that statistical data will be carefully interpreted. With the rapidly increasing numbers of older people, as well as with our changing community and family habits, it is going to be easy to quote figures that, if they are not carefully interpreted, may become the basis of ill-advised public action. Decreases in death rates are bound to be balanced by subsequent increases in other categories of the *International List*. Part of these increases must therefore be counted as compensating phenomena, and reckoned among the current landmarks of the constantly changing scene. The years of our lives are still approximately three score and ten. We have not increased the natural span; we have merely prevented infectious and metabolic accidents from snuffing us out prematurely.

It is to be hoped that gerontology may set a stage upon which a rational concept of aging processes will develop. Too often, in the past, we have been tempted by such plausibles as medical glandular and surgical rejuvenation. What has become of the operations of Voronoff and Steinhach? Such devices will fail for the same physiologic reason that Ponce de Leon failed in his quest for the Fountain of Youth. We badly need a basic science on which to build. For gerontology the field is open.



Lastly, it is to be hoped that practitioners of preventive geriatrics will not rush to establish for themselves examining and qualifying boards. None who is not a competent general practitioner can hope to become a competent geriatrician, and the time has come when a specialty for the general practitioner could have a salutary effect on medical values. Who better than the general practitioner could guide us across the falling ground and down into the valley? Those must be the years when the individual and family and community backgrounds will mean the most; those have been the years when the family doctor has served the best—let him now perfect himself. He is apter to have known us through all the seven ages described by the melancholy Jacques, and such knowledge is destined to be an important part of geriatrics.

And so from hour to hour we ripe and ripe,  
And then from hour to hour we rot and rot,  
And thereby hangs a tale

## UNITED CHINA RELIEF

THE Medical Division of United China Relief has announced the appointment of Dr. Co Tui as medical adviser to the China Defense Commission, which is in charge of all purchases for the Chinese government under the terms of the Lease Lend Act. A total of \$228,721 has been allocated for medical and relief supplies to free China; this sum was collected through the Bowl of Rice parties in California and through the tireless efforts of the national committee of United China Relief and the China Emergency Relief Committee. Dr. Co Tui, with the advice and help of leading American surgeons and physicians, will co-ordinate requests for medical provisions from medical experts in China and will help decide which supplies will most effectively meet Chinese needs.

The tremendous program of medical relief calls attention to facts that are frequently overlooked in the campaign of all out aid to Britain. China, too, has for years been resisting the aggression of an Axis power, and the Chinese government and

people deserve the fullest possible aid from the democracies. All-out aid to China is a contribution to the front line of American defense, medical aid to China will carry sorely needed relief not only to the inhabitants of Chungking, the most thoroughly bombed city in the world, but also to the millions who fight ceaselessly by day and night for the preservation of their country and the vindication of their national honor.

## MEDICAL EPONYM

### JARISCH-HERXHEIMER REACTION

Professor O Jarisch (1850-1902), of Graz, discussing "Therapeutische Versuche bei Syphilis [Therapeutic Experiments in Syphilis]" in a series of articles, writes as follows in his first installment, in the *Wiener medizinische Wochenschrift* (45: 721-724, 1895)

The following experiments were based on an observation that has certainly been made previously by many syphilologists, but has never to my knowledge been taken account of. I refer to the observation of a kind of reaction that shows itself in the first few days of a course of mercury inunctions in patients with syphilitic roscolae as an exacerbation of the topical phenomena of the disease. After from two to five inunctions or injections, the individual spots often become more distinct than before, and thus seem to be increased in number. This exacerbation of signs ends in an involution that, it seems to me, corresponds in rapidity to the intensity of the reaction.

If, as indicated by numerous facts, the effect of mercury in syphilis is not due to a supposed direct antiparasitic effect, the preceding fact must suggest the conception that mercury has an (indirect ?) chemotactic, inflammatory effect analogous to tuberculin and the bacterial proteins.

Dr. Karl Herxheimer (b 1861), chief physician of the Skin Department of the Municipal Hospital in Frankfurt am Main, and his assistant, Dr. Krause, contributed a paper, "Ueber eine bei Syphilitischen vorkommende Quecksilberreaktion [A Mercury Reaction Occurring in Syphilitic Patients]," in the *Deutsche medizinische Wochenschrift* (28: 895-897, 1902). A portion of the translation follows:

Some years ago, one of us observed striking changes in the exanthem of syphilis after the administration of mercury. More than a year ago, we made a similar observation of a patient suffering with a macular syphilide, which renewed our interest in the subject. The exanthem had changed to such a degree within about twenty four hours after an initial inunction of 40 gm of gray mercury ointment that no characteristic of the original efflorescent, either of size, form or color, remained. The lesions were larger, had become elevated above the surface of the skin, had taken on

a bright-red color, and had rather the characteristics of an eruption of erythema exsudativum multiforme. After twenty-four hours, however, it had completely disappeared. . . . After we had observed the reaction in more than 60 cases and were in a position to study it, we believed that we could describe it as follows: It appears, as has been said, when a sufficient amount of mercury is completely absorbed for the first time. . . . If there is any single, distinctive feature of the phenomenon, it is the change in the syphilitic exanthem from a typical to an atypical form. . . . From what has been said, it seems justified to consider this a "reaction." This is developed by an oversensitiveness of the cell, which has been affected by syphilis toward mercury in such a way that mercury, by uniting with the cell, causes increased damage.

R. W. B.

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

#### CESAREAN SECTION AND PNEUMONIA FOLLOWED BY DEATH

A thirty-two-year-old para II presented herself at a surgeon's office desiring a cesarean section. She stated that she was at term. Her desire for operation was based on unpleasant memories of the first labor and operative delivery, which the baby survived. Apparently no attempt was made to ascertain the history of the first pregnancy.

The past history was irrelevant, and the prenatal care during this pregnancy had been inadequate. Cesarean section, performed on a date set by the patient, was by the low-transverse cervical route. She was etherized by a nurse, and there is no indication in the history of how the anesthetic was taken. Death occurred nine days later, apparently because of a postoperative pneumonia. There was no autopsy.

*Comment.* This case is reported solely to emphasize the seriousness of needless cesarean section. Any laparotomy carries certain hazards, and even in the hands of trained anesthetists, pneumonia may cause death. A physician who does not appreciate this possibility is remiss in his obligations to his patients. In this case, there was no obstetric indication for cesarean section, and death should be attributed to lack of medical honesty.

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, Secretary, 330 Dartmouth Street, Boston.

## CORRESPONDENCE

### "ACCOUCHEMENTS FOR AMERICA"

*To the Editor:* We Americans are divided about many things, but interventionists and isolationists are agreed on one thing at least, and that is that America must prepare to defend itself. We hear cries for speeding up of manufacture of all sorts of vehicles and weapons of war. We are told that we need more ships, more tanks, more aeroplanes. I have as yet heard no one mention the fact that we shall need more young men to sail the ships, drive the tanks, fly the aeroplanes. In other words, America also needs more babies! Instead of other true slogans, it might be well for American women in the position to do so to take "Accouchements for America" as their slogan. If Germany wins the war and proceeds to utilize the shipyards and other resources of Europe,—perhaps for an attack on this country,—it may mean that 1960 will be the year when our country's fate is at stake. In my opinion, we should do long-range thinking, and attempt to increase our potential army of that time right now. If our birth rate can be increased, we may be able to keep our place in a world that sees the dictators making frantic efforts to increase their populations.

We should not allow the so-called "newer races" to carry our burden in 1960. Most of these people have large families and are having their deliveries cared for by clinics. Apparently few of the wealthy, who can afford an unlimited number of children, are desirous of large families. I believe that physicians should co-operate to encourage large families among the other class—that is, the great independent, bill-paying middle class. In the last few years, hospitalization plans have helped.

We may soon have such things as a bachelor tax and subsidies given to young people to allow them to be married early. My reason for writing this letter is to suggest that we get the jump on the rest of the country and start the ball rolling by offering a definite plan to encourage new citizens.

The plan is as follows: each physician will announce to his patients that each couple's fourth delivery will cost only 75 per cent of the third; the fifth delivery 75 per cent of the fourth and so forth. For example:

Fee for third baby	\$100
Fee for fourth baby	75
Fee for fifth baby	55
Fee for sixth baby	40
Fee for seventh baby	30

Those who object to this plan on the grounds that the fee is not commensurate with the time and trouble expended on the case should consider the service a patriotic duty, and reflect that, at the present time, innumerable French physicians would gladly accept even more burdensome conditions if France could be once again a strong, free, prosperous and happy nation. Incidentally, this movement will be an investment in good will, which will mean a great deal for our profession when the now apparently providentially postponed battle for socialized medicine is again commenced in the postwar period.

FRANCIS H. HIGGINS, M.D.

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## A STANDARD ELECTROENCEPHALOGRAPHIC TECHNIC FOR THE LOCALIZATION OF GROSS INTRACRANIAL LESIONS\*

FREDERIC A. GIBBS, M.D.,<sup>1</sup> DONALD MUNRO, M.D.,<sup>2</sup> AND WALTER R. WEGNER, M.D.<sup>3</sup>

BOSTON

SINCE Walter<sup>1</sup> first reported his technic for the localization of intracranial lesions by electroencephalography, ample evidence<sup>2-8</sup> has accumulated to prove beyond question its value as a supplement to previously available methods. The present report describes and gives the results obtained with a standardized and simplified technic, which, it is believed, makes electroencephalographic localization a more practicable clinical procedure. Except for a master selector switch, which will be described later, the required apparatus is the same as that used by Williams and Gibbs.<sup>4, 6</sup>

### APPARATUS

The apparatus consists of three channels of undistorted amplification of all frequencies from 1 to 1000, with a voltage intensification of approximately ten million times, a noise level of less than 5 microvolts, and three ink writing oscillographs that record without distortion up to 80 cycles per second. The amplifiers should be so designed that they are independent of each other, that is, the signals on one channel should not affect the signals on either of the other channels.

One of us (F. A. G.), in previous reports with Williams,<sup>4, 6</sup> subscribed to the use of cotton pledget electrodes wet with salt solution and held on the head with elastic bands. Such electrodes have the great advantage of being easily placed in any desired combination of positions, but they are so liable, by shifting and drying, to produce artifacts resembling the disorder produced by a tumor that it seemed hazardous to use them in ordinary clinical practice. If the type of electrode introduced

by E. L. Gibbs is used, electrode artifacts can be greatly reduced or eliminated. Such electrodes are made by flattening a solder pellet on the end of a fine (34 gauge) enameled wire. This can be done by thrusting the bare end of the wire into a heated drop of solder and pressing on the drop while still hot. The flattened pellet should form a disk about 1 or 2 mm thick and approximately 5 mm in diameter. Contact with the scalp is made by covering one side of the electrode with a saline paste (Sanborn electrode paste). A detailed description of the precautions to be taken in applying such electrodes is given elsewhere.<sup>9</sup>

In localizing intracranial lesions, it is desirable to cover all accessible surfaces of the brain with electrodes. As a practical compromise, sixteen leads are sealed to the scalp and forehead, all more or less equidistant from each other (Fig. 1). They are arranged in four longitudinal columns in such a way that the first column, referred to as A, starts with Electrode 1 slightly anterior to the right temple; Electrode 2 is placed over the right inferior precentral area, Electrode 3 over the right inferior postcentral area and Electrode 4 halfway between the third and the right occipital pole. The next column, referred to as B, has Electrode 1 half way between the upper and lower limits of the forehead and directly over the pupil; Electrode 2 is in the right precentral region, about two thirds of the way from the mid line to Electrode 2 in Column A, Electrode 3 in the postcentral area about two thirds of the way from the mid line to Electrode 3 in Column A, and Electrode 4 slightly to the right of the occipital pole. Column C is the left hemisphere equivalent of Column B, and Column D is the left hemisphere equivalent of Column A.

Each electrode is connected by its 34 gauge enameled wire lead to a separate binding post on a

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This study was aided by a grant from the Rockefeller Foundation.

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junction box. The junction box is equipped with a master selector switch designed and constructed by A. M. Grass. By means of this switch, it is

and by Williams and Gibbs.<sup>5</sup> Slow waves such as are seen around an organic lesion are more or less sinusoidal and very often have some normal ac-

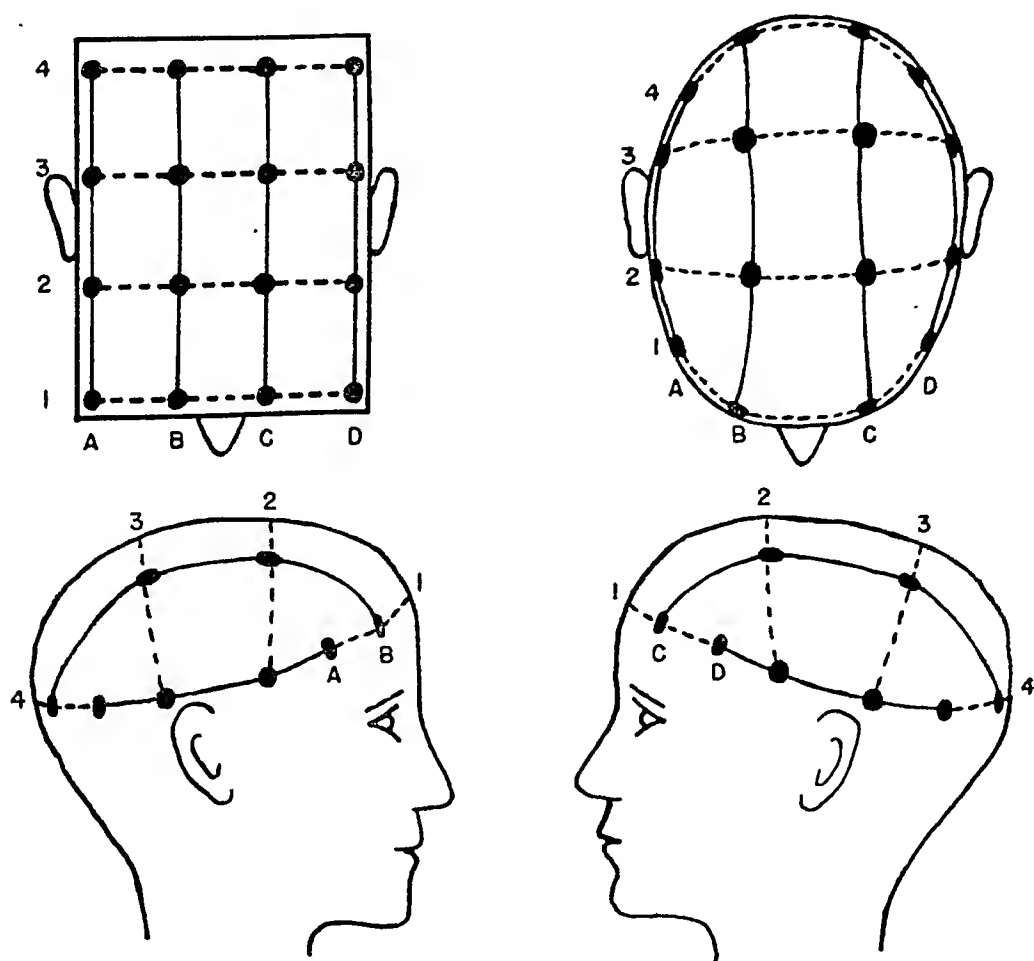


FIGURE 1. Diagrams Showing the Position of the Electrodes.

The diagram at the upper left shows the arrangement of electrodes on the schematized surface of the head, considered as a rectangle, with electrodes arranged in four equidistant columns, A, B, C and D, of four electrodes each and in four equidistant rows, 1, 2, 3 and 4, of four electrodes each. The other diagrams show the concessions that are made to the curved surface of the head in actual practice. The arrangement of the columns and of the rows is kept as nearly like the rectangular scheme as possible. The position of each electrode is described in the text.

possible to connect the amplifiers to any four electrodes, longitudinal or transverse, as shown in Figure 2.

#### CRITERION FOR LOCALIZATION

The criterion used for localization of gross organic lesions is that described by Walter,<sup>1</sup> namely, apparent reversal in phase of waves with a frequency of approximately  $\frac{1}{2}$  to 3 per second. Waves off this frequency Walter calls "delta waves." A region showing the maximal number and voltage of such waves (indicated by out-of-phase relations) he calls a "delta focus." Good illustrations of such foci are shown by Walter

and by Williams and Gibbs.<sup>5</sup> Slow waves such as are seen around an organic lesion are more or less sinusoidal and very often have some normal ac-

tivity superimposed on them. In general, the severer the lesion, the less the superimposed activity, the slower the waves and the higher their voltage. Extraneous voltage fluctuations, which might be confused with the slow waves from around a gross lesion, are discussed elsewhere.<sup>9</sup>

It is important to recognize at the outset that the apparatus cannot distinguish accurately between different types of lesion and that it cannot localize deep cerebral and subtentorial lesions. Smith and his co-workers<sup>10</sup> have said that subtentorial lesions can be localized with the electroencephalogram, but this is qualified to mean that

cases with cerebellar tumors show slow-wave foci in the occipital cortex. In our experience, such foci are usually lacking. Certain wave formations are commonly encountered in epilepsy. These have been discussed and illustrated elsewhere.<sup>3</sup> As pre-

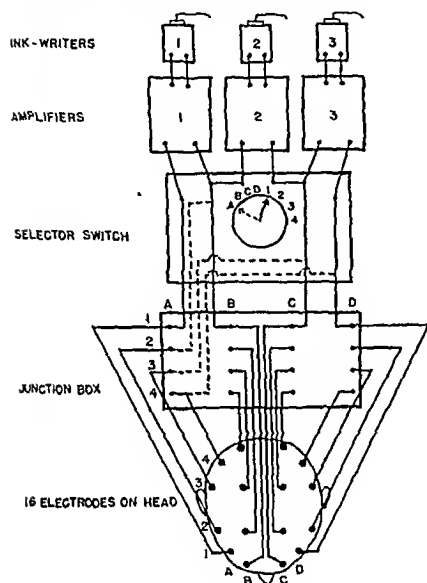


FIGURE 2 Schematic Diagram of the Manner in Which the Electrodes are Connected

By turning the dial on the master selector switch to any one of the indicated positions, A, B, C, D, 1, 2, 3 and 4, it is possible to connect the corresponding column or row to the amplifiers. When turned to a column (as shown by the dotted lines), Electrodes 1 and 2 go to Channel 1, Electrodes 2 and 3 to Channel 2, and Electrodes 3 and 4 to Channel 3, when a row is connected (as shown by the solid lines), Electrodes A and B go to Channel 1, Electrodes B and C to Channel 2, and Electrodes C and D to Channel 3.

viously stated, they are not generally satisfactory for localizing gross disease. However, any focus of epileptic discharge should be noted, for its presence and position—when taken with the rest of the clinical and laboratory evidence—may be a valuable diagnostic clue.

If a focus has been localized to the region under one electrode, the electrode should always be replaced with another close to it to make sure that a bad contact is not producing the slow waves.

If a focus cannot be detected with the primary

placement of electrodes, and if the clinical signs point to a specific area, all sixteen electrodes should be placed so that they form a square covering and extending beyond the presumable site of the lesion.

When the electroencephalographic localization is the sole or chief reason for contemplating surgical exploration of a particular area, it should be repeated on a subsequent day, with the sixteen electrodes concentrated around the region in which the focus was previously localized, to make sure that the focus is still there and to delineate it more sharply.

By concentrating the electrodes in a particular area, it is possible to get the maximum accuracy

TABLE 1. Results of Electroencephalographic Examination of 144 Patients Suspected of Having Operable Intracranial Lesions

RESULTS	No. OF PATIENTS
Examination revealed no focus	91
Discharged—insufficient evidence of operable lesion	83
Operated on	8
No gross lesion found	2
Deep cerebral or subtentorial lesion found	3
Examination revealed no focus	33
Discharged—insufficient evidence of operable lesion	15
Refused operation	3
Operated on	35
No gross lesion found	5
Gross lesion found	30
Focus not in same region as lesion	3
Focus in same region as lesion	27
Total	144

obtainable with electrodes placed on the outer surface of the skull. Grinker and Serota<sup>11</sup> have used electrode placements on the inferior surface of the cranium, and Jasper<sup>12</sup> has employed these electrode placements for localizing tumors. In certain cases, these so-called "nasal electrodes" may give important evidence. At any rate, the inferior surface of the brain is of interest in many clinical problems and should not be disregarded. However, temporal lobe tumors and tumors arising from the sphenoidal ridge can be localized with electrodes on the outer surface of the head. For clinical studies, it seems best to attempt first a localization with the sixteen electrodes covering the outer surface of the head and later, if additional evidence is required, to use special electrode placements, which are adjusted to the exigencies of the particular situation.

## RESULTS

The results of the electroencephalographic examination of 144 patients suspected of having gross intracranial lesions are shown in Table 1. In 33 patients with lesions found at operation, the neurologic examination led to a correct localization in 64 per cent, a ray study without air in-

jection in 21 per cent, x-ray study with air injection in 39 per cent and electroencephalography in 82 per cent.

The poor score for air injection followed by x-ray examination is not owing to any inaccuracy of the procedure but merely to the fact that because of discomfort to the patient, danger or expense, it was not used in the majority of cases. The true accuracy of the method appears when one considers the 14 cases in which it was used; it led to a correct localization in all except one case, that is, it was 93 per cent accurate. In the 10 cases in which no lesion was found at operation, a localized lesion was indicated by the neurologic examination in 7, by x-ray study without air injection in 2, by x-ray with air injection in 5 and by the electroencephalogram in 5.

### DISCUSSION

It is unlikely that any electroencephalographic method of localizing space-consuming lesions will give results as good as x-ray study with air injection, for the latter gives almost direct evidence of the lesion. On the other hand, electroencephalography is painless, without danger and relatively cheap, so that there is no reason why it cannot be used on all cases. It should be regarded as a special type of neurologic examination, which has the following advantage over the ordinary neurologic examination: it can test the functional activity of various cortical areas that are clinically silent. In the cases in this series that had gross supratentorial lesions, electroencephalography was more useful than urologic examination for localization. The comparative values and different methods of localization are discussed here to show how useful electroencephalography is in terms of other techniques now commonly employed, not with the idea that any of the latter should be abandoned. Ac-

curate localization of differently situated lesions of various types require the use of all available methods. Each method contributes to the total accuracy.

### SUMMARY AND CONCLUSIONS

A standardized and simplified form of Walter's technic for the localization of gross intracranial lesions is described, and the results obtained with it on a series of 144 patients suspected of having an expanding intracranial lesion are given. Of the 98 patients discharged because of insufficient evidence of an operable lesion, 85 per cent showed no electroencephalographic evidence of localized gross disease. Among the 44 patients operated on, electroencephalography gave correct localizations or correct negative findings in 73 per cent. In the 30 cases in which the lesion involved the cerebral cortex, localizations were accurate in 90 per cent.

The technic described is useful for providing evidence of the presence or absence of gross cortical lesions and for localizing such lesions.

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## TEMPORAL ARTERITIS\*

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UNTIL recently, the diagnosis of arteritis has been made in most cases by the pathologist. For this reason, the impression was gained clinically that all cases of arteritis and periarteritis were necessarily fatal. More careful observation of the superficial vessels has shown that arteritis and periarteritis are not only commoner and more widely distributed than was formerly believed, but that, in addition, the prognosis in certain types is distinctly favorable. During the last few years, arteritis of the superficial temporal vessels has emerged as a distinct clinical entity in which the prognosis is entirely favorable, even though the pathologic changes are indistinguishable from other types of arteritis. It has therefore seemed appropriate to report the cases of 3 patients who recovered from acute temporal arteritis, the diagnosis having been proved by biopsy.

## CASE REPORTS

**CASE 1.** M.B., a 58-year-old married woman, entered the hospital on July 2, 1940. She had been well until 3 weeks before admission, when she developed a severe headache along the right side of the forehead, the pain going down the right side of the neck. The pain soon spread to involve both sides of the head and neck, extending up to the top of the head and across the forehead. There was also a severe pain behind the eyes, and a marked paresthesia of the scalp, so that it was impossible for the patient to comb her hair. The past and family histories were noncontributory.

Physical examination on admission to the hospital revealed tenderness over both temporomandibular joints. It was impossible for the patient to open her mouth completely. There was some redness of the throat, the anterior pillars being more inflamed on the right than on the left. Small deep cervical lymph nodes were palpated on both sides, but no other lymphadenopathy was noted. There was exquisite tenderness over the temporal arteries on both sides. The heart, lungs, abdomen and reflexes were normal. The temperature was 101°F., the pulse 80, the respirations 20, and the blood pressure 118/62.

Laboratory examinations revealed negative blood Wassermann and Hinton reactions. The urine was normal. During the patient's 35 days in the hospital, the temperature varied from 98 to 103°F., with a tendency toward an afternoon rise. The white-cell count varied between 10,000 and 20,000, the majority of counts being approximately 14,000. Differential counts revealed 76 to 80 per cent neutrophils; the highest eosinophil count was 4 per cent, noted on only one occasion. The sedimentation rates were 62 and 70 mm. in 1 hour by the Wintrobe

method, the normal rate being 20 mm. The uric acid and nonprotein nitrogen levels of the blood were within normal limits. Agglutination tests for typhoid fever, paratyphoid (A and B) fever, brucellosis and tularemia and a sheep-cell agglutination test were negative, as was a gonococcus complement-fixation test.

Because of the possibility of meningitis, at the time of admission, a lumbar puncture was performed; the spinal fluid showed normal dynamics and pressure readings, a protein of 20 mg. per 100 cc., and 1 cell per cubic millimeter.

During the patient's stay in the hospital, she developed marked tenderness and induration over both temporal

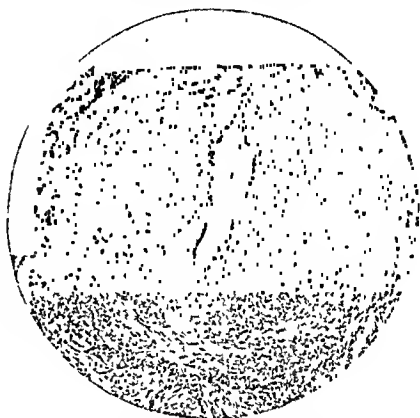


FIGURE 1. Photograph of Biopsy Specimen.

*This section shows the thickened wall and the narrowed lumen of the artery from Case 1 (eosin-methylene-blue stain,  $\times 55$ ).*

arteries, but no nodules. The severity of the tenderness changed from day to day and varied on both sides, as did the swelling over the temporomandibular joints. The frontal headache persisted, but could be alleviated by pressure over the temporal artery on either side. Codeine, morphine, Nembutal and phenacetin were used for temporary alleviation of the pain, but were not effective. On the 19th hospital day, sulfapyridine was begun, was continued for 4 days, and was discontinued because of marked nausea, vomiting and generalized discomfort. A free-sulfapyridine level of 7.4 mg. per 100 cc. was obtained, but there was no change in the patient's general condition or symptomatology.

On the 28th hospital day, a biopsy of the right temporal artery was performed under local anesthesia. On gross examination, the section showed some inflammation around the site of the temporal artery, and the artery

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appeared indurated. The pathological report was as follows:

The lumen of the vessel is diminished in caliber as a result of proliferation of the intima [Fig. 1]. The lumen is elongated, slender and lined by a single layer of endothelium, beneath which there is a large amount of fibrous tissue without inflammatory cellular infiltration. The internal elastic membrane is somewhat fragmented, but is not reduplicated. Within the muscular coat, chiefly in the internal longitudinal layer and in the outer circular layer of the media, but extending also into the adventitia, there are many small foci of cells resembling those of a granulomatous lesion. This area displays a central necrosis, with fibrinoid degen-

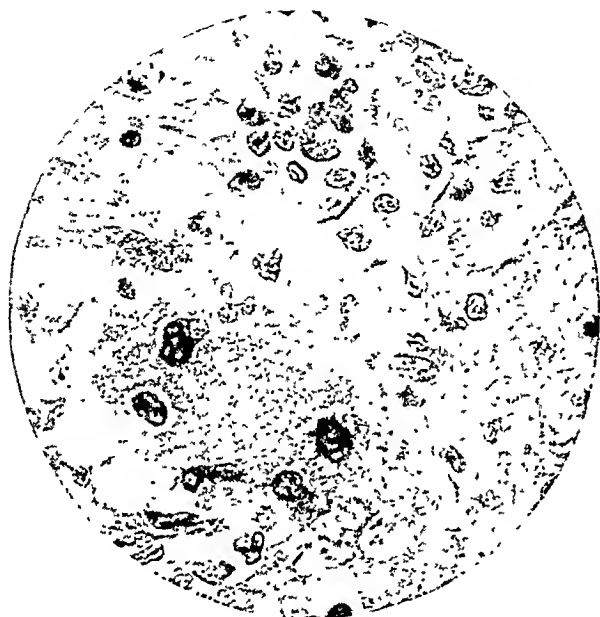


FIGURE 2. Photograph of Biopsy Specimen.

*This section shows a giant cell and the inflammatory infiltration in the wall of the artery from Case 1 (eosin-methylene-blue stain,  $\times 640$ ).*

eration. There are numerous multinucleated giant cells and large monocytes at the periphery of the section [Fig. 2]. In addition to these monocytes, the peripheral zone shows many lymphocytes mingled with some eosinophilic leukocytes and a few neutrophilic polymorphonuclear leukocytes. Careful search with various stains failed to reveal any micro-organisms. There is some increase in the fibrous tissue of the adventitia, and the smaller vessels in the surrounding fat are congested. Otherwise the fat and the striated muscle about the vessel are not remarkable.

The lesions in this vessel correspond to those described in cases of so-called "periarteritis nodosa" of the temporal artery. In our opinion, however, they bear more resemblance to the lesions in thromboangiitis obliterans (Buerger's disease) than they do to periarteritis nodosa.

Within a few days following the biopsy, the headache, paresthesia and tenderness were relieved, but the elevated temperature, increased sedimentation rate and leukocytosis persisted. The patient was discharged shortly after the biopsy was performed, and at present is symptom free. The blood counts and the temperature are normal.

The sedimentation rate, although still elevated, shows a tendency to be lower.

CASE 2. H.M., a 61-year-old widow, entered the hospital on April 20, 1939. Her complaints at that time were pain in the shoulders, hips, knees and back of 3 weeks' duration, and pain, swelling and tenderness around the temporomandibular joints of 2 days' duration. She also complained of severe generalized throbbing headache of about 3 weeks' duration. The past history and the family history were noncontributory.

When the patient entered the hospital, the temperature was  $100^{\circ}\text{F.}$ , the pulse 82, and the respirations 20. The blood pressure was 130/80. Physical examination revealed that the mandibular joints were tender, and that motion was limited by pain and swelling under both jaws. There was swelling of the lymph nodes in both submaxillary areas, but no other lymph nodes were enlarged. There were slightly red, indurated and tender areas over both temporal arteries. Pressure over the temporal arteries relieved the generalized frontal headache.

The blood Wassermann and Hinton reactions were negative. The urine was clear, and showed no albumin, sugar or casts. The white-cell count varied from 12,600 to 14,000, with 80 per cent neutrophils. Three per cent eosinophils were recorded on one occasion. Blood culture was negative. A skin test for tuberculosis with purified protein derivative of the first strength was negative. The basal metabolic rate was +12 per cent. The icteric index and an electrocardiogram were normal.

During the course of the illness, the patient remained comfortable on large doses of acetylsalicylic acid. The temperature varied from  $99$  to  $101^{\circ}\text{F.}$  The patient received a course of sulfanilamide for 8 days, during which she developed a marked gastrointestinal upset and an anemia. The red-cell count fell to 2,700,000. However, no essential change in the headaches or febrile course was noted. X-ray examination of the spine showed a moderate degree of arthritis.

On the 27th hospital day, a biopsy of the right temporal artery was taken. Microscopic examination of the section was reported as follows:

The artery shows marked chronic inflammation in all its coats. It is surrounded by chronic granulation tissue in which well-developed capillaries are seen, and in which proliferating fibroblasts are scattered from place to place. The entire area is densely infiltrated with cells that are predominantly lymphocytes, with a large number of monocytes, scattered polymorphonuclears, a rare eosinophil and occasional multinucleated cells that might be designated giant cells. A few lymphocytes extend into the muscular coat, separating the muscle bundles. The muscular coat is slightly thinned, and throughout its margin there are irregularly shaped masses of basophilic material, presumably fibrin. The intima is composed of proliferating connective-tissue cells, and only a minute lumen remains.

The headache disappeared to some extent after biopsy, but the patient was still febrile when she was discharged on the 32nd day.

A follow-up examination a year later revealed that the patient's elevated temperature and headache had almost completely disappeared, but she still complained of pain in the shoulders, hips, knees and back.

CASE 3. P.N., a 67-year-old store manager, was seen in the Out-Door Department on September 26, 1939. At that time, he complained of soreness and muscular aches



all over his body of 3 months duration. The patient also complained of generalized headache, pains around the mandibular joint and down the sides of the neck of 3 months duration.

The past history was significant in that the patient had had asthma presumably on an infectious basis for 5 or 6 years before this visit.

Physical examination revealed both temporal arteries to be enlarged and painful. The temperature was 98°F, the pulse 72, and the blood pressure 195/100. The rest of the examination was not remarkable. Without being referred into the hospital, the patient was anesthetized locally, and a partial excision of the left temporal artery was performed. The pathologic description of the section was as follows:

There is marked reduction of the lumen owing to intimal proliferation. Peripherally, the intima tends to be of a collagenous character whereas centrally it is more cellular and fibroblastic. A few lymphocytes and eosinophilic leukocytes are present throughout the intima. The internal elastic membrane is prominent. At some levels it completely surrounds the lumen, and at others it becomes imperceptible in an area of fibroblastic proliferation and inflammatory cell reaction. Throughout most of the circumference of the artery the normal parallel architectural arrangement of connective tissue and smooth muscle fibers of the media is well preserved. In some areas this arrangement is obliterated by an intense lymphocytic infiltration accompanying which there is a marked multinucleated giant cell reaction.

Postoperative recovery was uneventful.

When the patient was last seen, 1½ years later the headache and pain around the mandibular joints had practically disappeared.

### DISCUSSION

Historically, acute temporal arteritis has been mentioned in the literature since 1931. At that time, Horton, Magath and Brown<sup>1</sup> published a report of 2 cases. Since then, 16 additional cases have been reported.<sup>2-8</sup>

There is considerable similarity between the cases reported in the literature and our 3 cases. All the 19 patients reported have been elderly people, ranging in age from fifty-five to eighty years. The majority of the patients have been women. The presenting symptom is usually a severe, boring ache referable to both sides of the head, although usually severer on one side than on the other. The pain also seems to be severer at night, so much so that it prevents the patients from sleeping. In our experience, the headache is so intense that it is unrelieved by morphine or barbiturates. The temporal regions and temporal arteries may be tender, and during the course of the illness, the vessels may become enlarged, tortuous and surrounded by areas of hyperemia. Tenderness of the scalp and painful mastication may also be present—particularly prominent features in Case 1. In addition to the headache, the patient may complain of severe generalized symp-

oms. These patients often present the appearance of being severely ill, entirely out of proportion to the amount of local disease present. It is possible that the inflammation of the temporal artery is but a local manifestation of a more widespread disease.

The pathologic findings of the cases reported above are similar to those previously described. The general lesion is one of chronic periarteritis and arteritis. There are areas of granulation tissue in the adventitia of the blood vessels that suggest granuloma. There is an infiltration of round cells in the adventitia around the vasa vasorum, and to a marked extent in the media of the vessels. There may be a complete necrosis of the media, which is sometimes replaced by a granulomatous type of lesion. In all the cases in the literature and in our own cases, giant cells were present, and this seems to be a most constant factor. The lumen may be reduced in size, and nodular areas may appear along the outer aspect of the vessels.

From a practical standpoint the most effective treatment seems to be the removal of a segment of the temporal artery. This has been demonstrated in the 3 cases presented, and in 4 other cases in the literature.<sup>3,4,7,8</sup> After section of the artery, the headache is relieved, even though the fever and generalized symptoms may continue for as long as several weeks. It has been suggested that section of the artery severs the sympathetic nerve fibers<sup>6</sup> and in this way eliminates the pain although it is difficult to explain the ultimate relief of generalized symptoms with this treatment. It is worth noting that, in Cases 1 and 2, pressure over the temporal artery reduced the severity of the headache. This may be a point in determining whether section of the artery is going to be beneficial.

Because of the extreme practical importance of an accurate diagnosis before biopsy is undertaken, other common causes for the severe symptoms should be differentiated. First, there are intracranial causes such as brain tumor and meningitis and secondly, extracranial causes, such as phlebitis of the scalp veins, osteomyelitis of the malar and temporal bones, sinusitis, subcutaneous infection and herpes zoster. Biopsy of the temporal artery is justified in a patient with headache, fever, malaise, exquisite tenderness over the temporal artery and no other evidence of disease.

The cause of this localized arteritis is not known. Thromboses of the vasa vasorum might be an explanation,<sup>9</sup> but the reason for thromboses in this area is not apparent. Bacteriologic studies have been negative in all biopsy specimens. The fact that the pathologic specimens demonstrate

and 700 cc. of dark-red blood aspirated. Three weeks later, a second thoracentesis yielded 600 cc. of dark-amber sterile fluid. The operative wounds healed by primary union. During the 5th week of the patient's illness, the temperature hovered about 101°F. but dropped to normal within 48 hours after a third thoracentesis, which yielded 900 cc. of clear, yellow sterile fluid. The subsequent course was uneventful, the patient being allowed out of bed on the 45th day and discharged on the 50th day.

X-ray studies of the chest taken on admission and subsequently on the 1st, 4th, 12th, 19th and 21st days post-operatively revealed progressive changes consistent with the accumulation and resorption and aspiration of the pleural fluids.

Electrocardiograms were taken preoperatively (Fig.

1), during the operation (Figs. 1 and 2, B-M) and post-operatively (Fig. 3). The findings are discussed below.

*Q wave.* Tracing A reveals a deep Q wave in Lead 1. Beginning with a depth of 3 mm., it reaches a depth of 6 mm. in Tracing F, at the time of entering and aspirating the pericardial sac. The Q wave then recedes to a depth of 2 mm. when the chest cavity was finally closed (Tracings L and M). Subsequently, it remained between 1 and 2 mm., but was no longer 25 per cent or more of the main deflection. No other leads at any time showed an initial downward deflection.

*Electrical axis.* At the time of operation, when the deep Q wave was present (Tracing F), a right ventricular preponderance is noted. Subsequently, the deviation of the electrical axis became normal.

*P wave.* In Leads 1 and 3, in the tracings taken before and during the operation, the P waves are

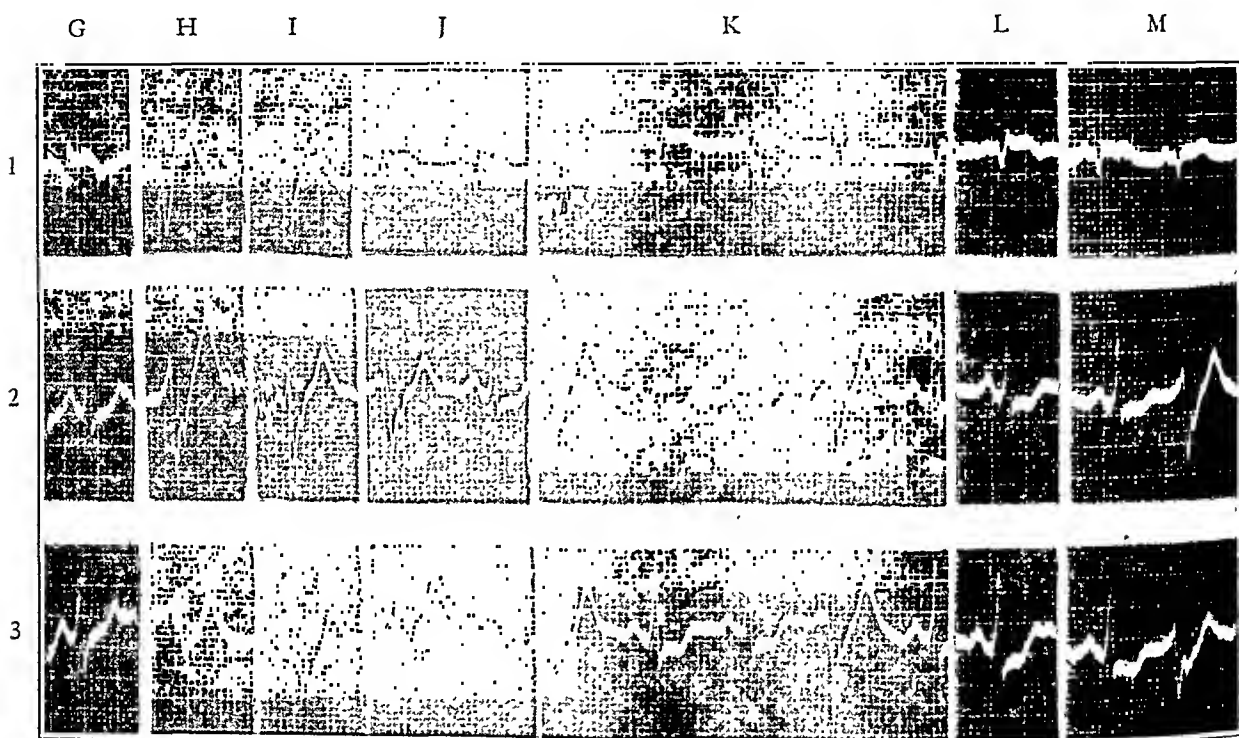


FIGURE 2.

1), during the operation (Figs. 1 and 2, B-M) and post-operatively (Fig. 3). The findings are discussed below.

#### ELECTROCARDIOGRAPHIC FINDINGS

*Rhythm.* The basic rhythm preoperatively and during the operation, as well as during the subsequent twenty-four hours, was a sinus tachycardia, with premature ventricular contractions and a ventricular rate of 120. After twenty-four hours, normal sinus rhythm ensued, with a rate varying between 80 and 100. Ventricular premature contractions were noted preoperatively and during the course of the operation. In Lead 1 of Tracing A, taken preoperatively, coupled rhythm is seen, each normal complex being followed by a ventricular premature contraction each of which shows a slightly different configuration suggesting a varying origin. In Lead 1 of Tracing D, the ventricular premature contraction has its main de-

*Q wave.* Tracing A reveals a deep Q wave in Lead 1. Beginning with a depth of 3 mm., it reaches a depth of 6 mm. in Tracing F, at the time of entering and aspirating the pericardial sac. The Q wave then recedes to a depth of 2 mm. when the chest cavity was finally closed (Tracings L and M). Subsequently, it remained between 1 and 2 mm., but was no longer 25 per cent or more of the main deflection. No other leads at any time showed an initial downward deflection.

*Electrical axis.* At the time of operation, when the deep Q wave was present (Tracing F), a right ventricular preponderance is noted. Subsequently, the deviation of the electrical axis became normal.

*P wave.* In Leads 1 and 3, in the tracings taken before and during the operation, the P waves are

20 to 30 mm in height, becoming 10 to 15 mm in height during recovery.

**PR interval** The PR interval was 0.12 second throughout the period of observation.

**QRS interval** The QRS interval in the normal complexes was 0.06 second throughout the entire period of observation.

**ST segment** ST<sub>1</sub> is elevated in the tracings taken at the beginning of the observation, and

**Lead 4** Preoperatively (no tracing shown), P<sub>4</sub> was inverted, S<sub>1</sub> prominent, and ST<sub>1</sub> depressed. Subsequently the P waves and ST segments became practically isoelectric, and T<sub>4</sub> small and inverted.

#### SUMMARY

A bullet wound of the heart involving a branch of the left circumflex artery supplying the anterior and lateral portions of the left ventricle was noted

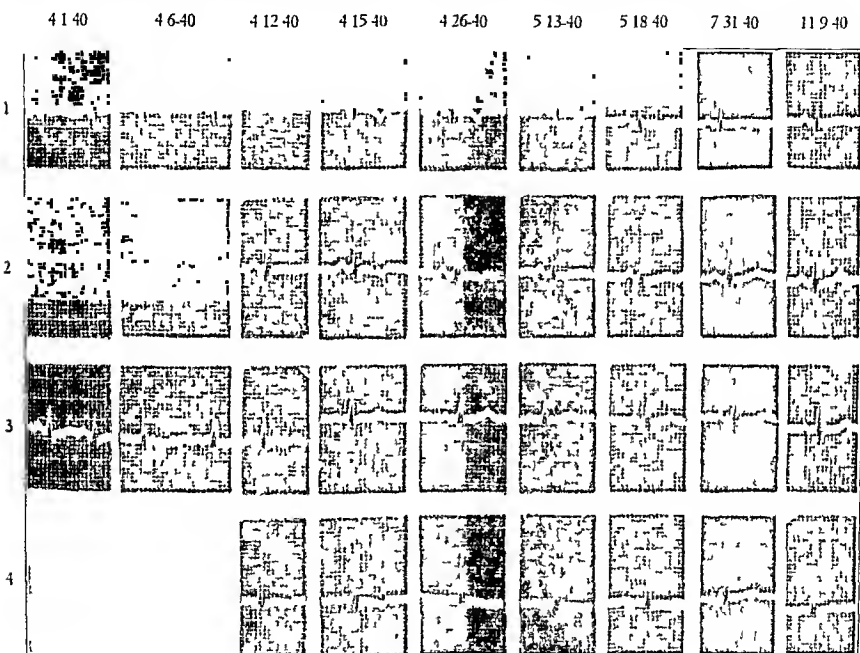


FIGURE 3

remains so in those taken during and one day after operation. Five days later, it became isoelectric and remained so thereafter. ST<sub>2</sub> was depressed before and during operation (10 to 20 mm). Postoperatively, it gradually reached a level about 0.5 mm below the isoelectric line. ST<sub>3</sub> changes were parallel with those of ST<sub>2</sub>.

**T wave** T<sub>1</sub> was inverted and became most apparent as the ST segment gradually became isoelectric. T<sub>2</sub> was upright, except for a period of about one month beginning twelve days postoperatively, when it was inverted. T<sub>3</sub> remained essentially upright throughout, although the depressed ST<sub>3</sub> segment at times obscured the interpretation

to be associated with the following electrocardiographic findings. Ventricular premature contractions arising in several foci were superimposed on normal sinus rhythm and sinus tachycardia. The premature contractions occurred both sporadically and at regular intervals, varying from coupling to tripling and quadrupling. The configuration of the premature contractions noted most frequently corresponded to that expected from the site of the injury. Q<sub>1</sub> became sufficiently deep at one period to cause deviation of the electrical axis to the right. No conduction defects were noted. ST changes corresponded to effects found in cases of coronary thrombosis with infarction.

T<sub>1</sub> became inverted—the most notable change.

It appears that in this case the preponderant effect on the electrocardiogram resulted from myocardial injury with necrosis, although definite pericardial disease was also known to be present.

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## NEW HAMPSHIRE MEDICAL SOCIETY

### PROCEEDINGS OF THE ONE HUNDRED AND FIFTIETH ANNIVERSARY

House of Delegates, May 12, 13 and 14, 1941

(Concluded from the issue of July 24)

The work of the committee was approved by the Committee on Officers' Reports, and Dr. D. G. Smith urged that members attend the New England Postgraduate Assembly and take advantage of the Commonwealth Fund Fellowships; the report was adopted.

Dr. Charles H. Dolloff then read the report of the Committee on Mental and Social Hygiene.

#### *Report of the Committee on Mental and Social Hygiene*

The Committee on Mental and Social Hygiene has no special recommendations to make this year, and believes the Society should be given the opportunity to catch up on what has already been recommended in years past.

Demands are constantly being made for enlargement of the mental-hygiene program, with the establishment of more clinics in the larger centers, but the influence of the Society does not appear to be brought to bear on those who would be able to furnish the necessary money. The need of an extension of social service as part of the prophylactic program is obvious, but languishes for lack of support.

One of the outstanding contributions to the program of mental and social hygiene is the survey sponsored by Ex-Governor Huntley Spaulding.

Mental hygiene and social hygiene are primarily public matters, and must stand or fall according to the amount of public support they receive. It would be of great help if the force of this large body of physicians, through a legislative committee, could be put behind the legislation required for these public projects.

Right now our state institutions caring for the mentally afflicted are suffering from the dearth of good physicians and other employees, owing to their inability to pay adequate salaries and wages.

A medical and surgical building is being constructed

at the State Hospital, and the State School is about to open bids for the construction of another dormitory.

CHARLES H. DOLLOFF  
BENJAMIN W. BAKER  
JOHN B. McKENNA

Dr. D. G. Smith, of the Committee on Officers' Reports, recommended that the Committee on Public Relations be asked to watch for and to support bills in the legislature that provide for the improvement and extension of the mental-hygiene program and moved the adoption of the report; it was so voted.

The next report was that of the Committee on Tuberculosis.

#### *Report of Committee on Tuberculosis*

"A Good X-Ray Is Your Doctor's Best Aid in Discovering Early Tuberculosis" is the theme of the fourteenth annual nation-wide Early Diagnosis Campaign conducted in April each year by the tuberculosis associations throughout the nation.

For several years in this campaign the chest x-ray has been stressed as the correct diagnostic method for finding tuberculosis in its early, most curable stages. But this year, the x-ray looms as a great defense weapon, for it is the recognized means of ensuring that tuberculosis is kept out of the military forces of the country.

In World War I the main reliance was the usual diagnostic procedure—inspection, percussion and auscultation. Today it is known that this reliance resulted in rejection and discharge of but one eighth of the tuberculous subjects called into the service. Is it any wonder that the expenditures for hospitalization, compensation and rehabilitation for tuberculosis among the veterans is today entering the second billion of dollars by the federal government?

Today, through the program of chest x raying of national guard men and selective service men in New Hampshire, the federal government has been saved at least \$150,000 in eventual charges for tuberculosis.

Beginning with the induction of the 197th Regiment, Anti Aircraft, at Concord on September 16, 1940, and up to March 1 of this year, a total of 3167 national guardsmen and selective-service men have been chest x rayed at the Concord camp grounds, the state armories and the new induction center in Manchester. Of these men, 15 were rejected because of evidence of tuberculosis of the lungs, and several other men were deferred because of diseases of the chest revealed by x ray study.

It is difficult to total the costs of this service because of the fact that the staff members of official and nonofficial health agencies carried out the program in co-operation with the induction agencies, yet it is estimated that the cost did not exceed \$2500. This particular service is cited as an index of the tremendous value of the x ray in searching out the smallest evidences of the presence of tuberculosis of the lungs.

The tuberculin test is more and more demonstrating its value as an aid in the diagnosis of tuberculosis. With rapid reduction in the number of positive reactors to the test, its value as a screen in sifting out those harboring infection with tuberculosis bacilli becomes increasingly evident.

The value of tuberculin testing and chest x raying of positive reactors among contacts of tuberculous patients is well recognized.

More frequent use of the tuberculin test and chest x ray by physicians in their offices and in the hospitals can materially aid in early diagnosis.

New Hampshire continues to maintain an enviable position with reference to its tuberculosis death rate. The reduction in rate has been persistent and phenomenal, from 97.8 per 100,000 population in 1920 to 28.47 in 1939.

Many factors no doubt have and are contributing to the control and advance toward eradication of the disease in New Hampshire—better living and working conditions, the cure of many tuberculous patients through more prompt and better treatment, and the reduction in numbers of new cases developing through the destruction of tubercle bacilli at their source among the afflicted.

The sanatoriums at Glencliff and Pembroke report encouraging increases in numbers of patients receiving pneumothorax treatment. Technical improvement has given better results and fewer complications. Gratifying effects continue to be evident in patients receiving chest surgery. The generous and wholehearted cooperation of our chest surgeons and the hospitals has made possible arrest of the disease in certain patients for whom there could be but a future of chronic invalidism and ultimate disaster. This service has been performed at a minimal cost only through the generous spirit of cooperation already mentioned.

A difficult problem continues to exist in the necessity of providing for sanatorium treatment for tuberculous patients in accordance with present day standards of strict bedrest over long periods of time. The infirmary facilities at the Glencliff Sanatorium have been taxed to the utmost. Empty beds are present in the cottage wards but cannot be used except for convalescent patients, because of their inadequacy for hospital treatment and care.

The grateful appreciation of all concerned is extended to the practicing physicians of New Hampshire for their increasingly effective co-operation, particularly their willingness to urge and provide chest x ray films through the

hospitals at a nominal cost for clinic cases. The officers and directors of the New Hampshire Tuberculosis Association, the examining physicians at the chest diagnostic centers, the field nurses, the patients and the public join in this expression of appreciation. It is keenly realized that this generous sympathetic understanding and assistance on the part of our physicians is due to the keen desire of the members of the New Hampshire Medical Society to hasten the eradication of tuberculosis among the people, and to confidence in the services of the chest diagnostic clinics.

Your committee urges more use of the tuberculin test, either the Mantoux, using protein purified derivative, or the Vollmer patch test. We urge this for all contacts with tuberculosis, for all patients presenting suspicious symptoms or signs, in fact for all chronic coughers, losers of weight and tired people. We urge chest x ray for all positive reactors to the tuberculin tests.

Your committee is glad to be of assistance in the interpretation of chest x ray films sent to them by any member of the Society. This service is increasing, yet we urge more and more use of it.

ROBERT B KERR  
ROBERT M DEMING  
M DWYSON TYSON

On the recommendation of the Committee on Officers' Reports, the report was adopted.

Dr Parsons, chairman of the Committee on Memorials and Communications then presented four communications for consideration. The first was from the State Board of Health and concerned a proposed survey to determine the incidence of syphilis in low wage groups, to be undertaken with the co-operation of certain large industrial plants, some discussion followed, but no action was taken. The second was a resolution submitted by the New Hampshire Maternal Health Association, Incorporated, which read as follows:

WHEREAS, The American Medical Association at its Annual Convention in June, 1937, defined birth control as an integral part of preventive medicine and adopted a four point program to provide for scientifically tested methods of contraception and instruction in their use, the four points being to inform physicians clearly about their medical rights, to carry on research in materials and methods for the prevention of conception, to promote thorough instruction in contraception in medical schools, and to bring all dispensaries, clinics, and similar establishments under legal licensure and medical control, therefore, be it

RESOLVED, That the New Hampshire Medical Society endorses the stand taken by the American Medical Association and recognizes the need for medically supervised contraception as an integral part of preventive medicine.

The third was a communication from the American Medical Association concerning the hospital construction bill (No 1230) introduced into the United States Senate, the committee recommending that approval be extended, provided that construction be limited to that proved to be urgently

needed and that adequate maintenance be assured; this recommendation was adopted, as well as a supplementary one creating a special committee to act in an advisory capacity to the executive office of the State Board of Health on any contemplated hospital-construction project under this pending legislation.

It was voted to take off the table the motion in regard to the creation of a committee on public health; and it was then voted to create a new standing committee, the Committee on Public Health, consisting of three members. Subsequently, the tabled motion that the Committee on Public Health be instructed to consider the problem of the State Laboratory as a real competitor of the clinical pathologists was taken off the table and was approved. Furthermore, the accepted motion creating an advisory committee in regard to hospital construction was amended so that the matter was referred to the Committee on Public Health.

The final communication presented by the Committee on Memorials and Communications was a letter from the New Hampshire Farm Bureau Federation in regard to the formation of a co-operative to underwrite the costs of medical care to low-income groups in rural areas. Since accurate facts concerning the need for such a plan are lacking, the committee recommended that a special committee be appointed by the President to co-operate with representatives of the Farm Bureau in a thorough investigation of the problem. Dr. D. G. Smith, of the Committee on Officers' Reports, moved that part of the recommendation creating the appointment of a special committee be not accepted, that the rest of the recommendation be accepted and that the matter be referred to the Committee on Medical Economics, as had the question of enabling legislation covering medical-care insurance; it was so voted.

Dr. Benjamin P. Burpee then presented the report of the Committee on Infancy and Maternity.

### *Report of the Committee on Maternity and Infancy*

This is the seventh year during which the Committee on Maternity and Infancy of the New Hampshire Medical Society has conducted a study of maternal deaths, infant deaths and stillbirths that occurred during the preceding year. The study, as in the past, is an effort to analyze the causes of maternal deaths and to appraise, so far as possible, the problems relating to the causes of deaths among mothers and babies. All agree that, although the maternal death rates in New Hampshire and in the United States as a whole have shown an encouraging downward trend, there are still too many mothers

and too many infants under one year of age who die needlessly each year.

The committee has endeavored to collect as complete data as possible on each maternal death reported, and has analyzed the facts obtained with as impartial but scrutinizing care and judgment as is possible in cases where only abstract material is considered. No absolute or arbitrary conclusions can be drawn from such a study, but one can evaluate the cold facts in each case and suggest alternative procedures that might have aided in preventing the death. All this, of course, is done with the advantage of retrospect and without the element of the personal responsibility and emergency factors experienced by the physician in actual charge of the case.

The committee's remarks and conclusions must be understood at the outset to be entirely impersonal, since the name of the physician, the name of patient, the location of death and other identifying information are never known to the committee members. Only one person acting as agent must of necessity know these facts in order to collect the necessary data. That person is the director of the Maternal and Child Health Division of the State Board of Health. The study this year, as in the past, has been carried on with the co-operation of the Division of Maternal and Child Health of the State Board of Health.

Since the annual meeting of the Society last year the committee has held five meetings. These were as follows: November 20, 1940, and February 19, March 5, April 16 and April 28, 1941.

At each meeting the committee studied carefully the information collected on each case and considered every phase of the problem. Materials used in gathering data consisted of a copy of the death certificate, answers to questionnaires sent to the physician who signed the death certificate, and in most cases, facts gathered by personal interview of the agent with the physician and data from the hospital record. All cases were studied by number and all correspondence was transmitted through the Division of Maternal and Child Health.

After the cases were studied a letter was sent to the physician reporting the case, giving the committee's comments and whatever important suggestions the committee felt would be of interest or value. In some cases quite an interesting correspondence ensued between the physician and the committee, via the Division of Maternal and Child Health, in which frank comments were made from both sides. This seems to be a most wholesome practice, since out of such a medium of debate and study some excellent educational and helpful suggestions are bound to spring. The committee believes that much mutual benefit has been secured by this means.

Regarding the study of infant deaths under one year, the committee thought that the best that could be done was to reappraise these deaths as to causes reported. There were too many infant deaths reported to enable the committee to secure full data on all. Therefore, in the following pages a tabulation of causes will be set forth and some conclusions drawn.

Stillbirths were analyzed also from the standpoint of causes. Questionnaires were sent out to physicians reporting stillbirths, and excellent co-operation was obtained in the returns. A tabulation of chief causes will follow in the report.

### MATERNAL DEATHS

The committee has tabulated the maternal deaths for the calendar year ending December 31, 1940, according to the *International Classification for the Causes of Deaths*

(fifth revision) There were 24 maternal deaths reported, and all were studied. Following an appraisal of each case, the committee then reclassified the deaths into categories of causes according to the data received and conclusions drawn from that data, as follows

CODE NO	CAUSE OF DEATH	NO OF DEATHS
140	Abortion with mention of infection	3
142 (b)	Ectopic gestation (without mention of septic conditions)	1
146 (c)	Post partum hemorrhage	4
147 (b)	Puerperal septicemia (not specified as abort on)	1
147 (d)	Acute pulmonary embolism	3
148 (a)	Puerperal eclampsia	3
148 (b)	Mild toxemia of pregnancy	1
149 (b)	Other accidents of childbirth	3
	Cesarean section	1
	Myocardial infarction	1
	Heart failure	1
		24

After thorough study of each case, taking into consideration the events leading up to the death of the patient, the past history and the hospital record, the committee reclassified the cases as to causes of deaths, as follows

CAUSE OF DEATH	NO OF DEATHS
Toxemia of pregnancy (eclampsia and mild toxemias)	8
Cesarean section with complication (without consideration for indications)	1
Post partum hemorrhage	4
Puerperal sepsis	1
Causes not due to pregnancy	2
Cardiac failure	2
Accidents of pregnancy	3
Pelvic thrombosis with embolism	2
Ectopic pregnancy	1
Abortions	3
Unclassified	2
	24

Cases were further classified into three categories,—Group I, those in which the patient was at fault, owing to neglect, failure to seek medical advice prenatally and so forth, Group II, those in which the obstetric treatment was inadequate, Group III, those which were apparently unavoidable,—as follows

CLASSIFICATION	NO OF DEATHS
Group I	3
Group II	9
Group III	10
Unclassified	2
	24

In the unclassified group, one record was incomplete, and one death was not deemed to have been due to maternal causes

The causes of death in Group I, in which the patient was at fault, were as follows

CAUSE OF DEATH	NO OF CASES
Induced abortion	1
Toxemia of pregnancy (no prenatal care sought)	1
Hemorrhage (stony uterus—patient in extremis when seen)	1
	3

The causes of death in Group II, in which the obstetric care was inadequate, were as follows

CAUSE OF DEATH	NO OF CASES
Cesarean section	1
Criminal abortion	2
Eclampsia	3
Post partum hemorrhage	2
Pelvic thrombosis with pulmonary embolism	1
	9

The causes of death in Group III, in which the deaths were apparently unavoidable, were as follows

CAUSE OF DEATH	NO OF CASES
Intestinal obstruction	1
Eclampsia (cesarean done in 1 case)	4
Pelvic thrombosis	1
Pelvic abscess (furunculosis)	1
Ectopic pregnancy	1
Cardiac failure	2
	10

In comparison with the study of 1939 deaths, it is interesting to note that toxemia of pregnancy was still the chief cause of death. Only three fatal cesarean sections were performed, in contrast with five recorded for 1939. Two of these sections were deemed responsible for the patients' deaths, the other was done on a patient with marked toxemia, and the death was considered to have been due to the toxemia rather than to the operative procedure per se.

In the 1940 series, 23 cases were delivered in hospitals and 1 in the home. The following data on urban and rural residency are also of interest

COUNTY	URBAN CASES	RURAL CASES	TOTAL CASES
Bellamy	2	0	2
Carroll	0	1	1
Chester	0	1	1
Cook	1	0	1
Grafton	1	2	3
Hillsborough	8	2	10
Merrimack	1	0	1
Rockingham	3	0	3
Stratford	1	0	1
Sullivan	2	0	2
	19	5	24

No study is of value unless it is compared with findings of previous years. There were a few noticeable improvements found this year over those of last, and some conditions remained about the same. It is worthy to note that the co-operation manifested by physicians in reporting findings, giving data and answering questionnaires was greatly improved. Of twenty four questionnaires sent out, all but one were returned, with excellent and complete data. When visited, the physicians showed a genuine interest in the study and were most anxious to discuss all features of the case.

As indicated above, only three cesarean sections were performed, as compared with five for the previous year. Five autopsies were performed in 1940, however, as compared with six the year before. Indications for post mortem examinations varied somewhat in the two years, since more cases were due to definite causes this year. The committee believes, however, that whenever there is a doubt of the cause of death, an autopsy should be secured, if possible.

Hospital records were more complete than in former years, and it was noted with gratification that more physicians made out their own records instead of depending on hospital nurses to do so.

There is still a great deal to be desired in reference to hospital staffs requiring consultations on all operative deliveries. There has been a noticeable improvement in hospital technique and equipment. In some hospitals, new nurseries have been installed, which are well equipped for the isolation of infants. Other hospitals have secured incubators, put on fire escapes, unproved plumbing facilities and sterilizing equipment and so forth. This forward movement on the whole is encouraging and is a trend that the committee believes is due to more efficient hospital administration and better co-operation with public health agencies.

The ever-discouraging feature of any study on maternal deaths is the fact that toxemias of pregnancy continue to lead the list of all causes listed. Particularly discouraging is the fact that even when a diagnosis of toxemia of pregnancy is obvious from the records, little seems to be known by most physicians as to the treatment. Either very inadequate and futile "stabs in the dark" are made in treatment, or else no treatment is given. Not one case of toxemia studied in 1940 could be deemed as having been treated adequately.

The committee realizes that the treatment of toxemias of pregnancy is a controversial subject. Nevertheless, this fact seems to be no excuse for lax treatment of the patient with toxemia. The committee believes that patients with mild toxemias are allowed to go too long without proper treatment. A persistent rise of blood pressure over what is known to be the patient's normal pressure before pregnancy should be considered evidence of toxemia, even in the absence of albumin in the urine. Because of the persistent problem arising out of uncertainties in the treatment of toxemias, the committee will include in its recommendations a simple outline for the treatment of toxemias (this was included in the 1938 report). Let it be understood that the committee does not set itself up as an infallible authority in this matter, but believes the suggestions may prove of value to some.

The committee has presented an analysis of maternal deaths as to causes and as to facts that might be of interest as contributing to the death of the patient. It may be well to include at this point a tabulation of maternal death rates for a series of past years in order to note the trend in maternal mortality statistics:

YEAR	NO OF DEATHS	MATERNAL MORTALITY RATE PER 1000 LIVE BIRTHS
1930		62
1932		54
1933		63
1934		54
1935	46	61
1936	37	46
1937	34	43
1938	24	38
1939	25	31
1940	24	28

It will be noted that, up to 1936, maternal death rates had no appreciable variation. From 1936 on, the rates show a steady downward trend. This is probably not statistically significant as yet, owing to the smallness of the series of years. However, since New Hampshire's birth rate has remained almost constant for many years, such a downward trend, if continuous, will no doubt prove significant. The committee would like to think that this downward trend is due to better obstetrics or at least to concerted efforts on the part of the medical profession to improve technics at the time of delivery and to better prenatal care. Time alone can tell, and efforts must forever be strengthened. As yet it is not wise or logical for the profession to take much credit regarding the lowered mortality rates in maternity.

INFANT MORTALITY

The study of causes for infant deaths under one year was conducted by the committee from data appearing on the death certificates only. The large number of infant deaths reported did not permit an exhaustive analysis. However, the committee has tabulated infant deaths by causes as they appeared on the death certificate. The ages at which the deaths occurred were separated into three periods

It is obvious again, as in former reports, that prematurity was by far the chief factor leading to the death of the newborn. There was an improvement in the reporting of causes of deaths this year over that of 1939, fewer vague and meaningless diagnoses being recorded. Twenty-one autopsies were performed. This is a distinct improvement over last year. Following is a tabulation of causes of death in infants under one year of age divided into periods as to when the deaths occurred:

CAUSE OF DEATH	NO. OF DEATHS
Deaths occurring during the first day of life	
Prematurity	75
Congenital malformations	14
Cerebral hemorrhage	7
Birth injury	7
Asphyxia	2
Syphilis	1
Atelectasis	4
	110
Deaths occurring in the first month, exclusive of the first day	
Prematurity	21
Congenital malformations	10
Intracranial hemorrhage	7
Birth injury	5
Pneumonia	4
Gastroenteritis	3
Hemorrhagic disease of newborn	3
Whooping cough	2
Enlarged thyroid	1
Unknown	1
	57
Deaths occurring from the second to the twelfth month, inclusive	
Bronchopneumonia	49
Suffocation	9
Congenital heart	7
Meningitis	7
Gastroenteritis	6
Congenital malformations	6
Malnutrition	5
Prematurity	5
Unknown	5
Accidents	4
Congenital syphilis	1
Intussusception	1
Blood dyscrasias	2
	107

The total number of infants who died in 1940 under one year of age is 274; this is 33 less than that for 1939, when 307 infants died.

The total deaths from prematurity for 1940 numbered 101. It will be seen from the table that 75 of these infants died during the first day of life. Since such an astounding number of infants are lost owing to prematurity, it may be well to outline briefly a few important considerations in the care of the prematurely born infant. The committee believes that prematurity as a cause of death is, in many cases, preventable. The mere fact that an infant is born with a birth weight of 5½ pounds or less seems little excuse for the infant's death, provided, of course, that the infant has sustained no cerebral injury, has attained viability, and is in all other respects free from deformity or abnormality. The care of the premature infant involves, therefore, the following principles:

1. Extreme care should be exercised by the physician, nurses and attendants at the time of delivery to avoid trauma, unnecessary exposure or rough handling. "Jackknifing" as a method of resuscitation is condemned. Diagnosis before the onset of labor or during labor as to the possibilities of a premature infant should be attempted, and proper planning for the delivery should be considered. Teamwork practiced by the doctor, mother and nurse is essential to afford the best outcome. Equipment for resuscitation of the infant should be available at the time of de-



livery, and means for maintaining normal body temperature should be at hand. Time is a most important factor in the care of the newborn premature infant. Most of them die during the first few hours after birth and during the first day. After the first day, the infant has an increasingly good chance for life.

2 During labor, barbiturates should be cut down to a minimum. Premature infants do not tolerate sedation, particularly by barbiturates, and many infants born prematurely cannot be resuscitated under conditions in which the mother was given the usual dosage of barbiturates.

3 The maintenance of as nearly normal body temperature as possible is essential. Avoidance of excessive temperature should also be considered. An improvised heated crib built of simple materials and designed to keep fairly constant temperature is satisfactory. Heat can be provided by the use of hot water bottles or by a protected electric light bulb. A thermometer should be available to check the temperature of the crib at frequent intervals. (Plans for such a heated crib can be obtained from the committee or from the Division of Maternal and Child Health of the State Board of Health on request.)

4 Careful and scrupulous attention should be paid to avoidance of infections, particularly upper respiratory infections. Attendants should wear masks at all times.

5 Extreme care should be taken to provide adequate and proper nursing care and supervision of the premature infant. The physician should supervise all phases of the care, including feeding, handling and any special treatment. Transfusions are at times necessary. Handling of the infant should be reduced to an absolute minimum, and avoidance of drafts, changes of temperature and so forth should be considered.

6 Recent and studied observations have shown the definite value of the use of vitamin K at the onset of labor. It is a well known fact that the prothrombin concentration of any newborn's blood drops markedly almost immediately after birth. This is, in some cases, responsible for cerebral hemorrhage or bleeding. This fact is particularly of significance in the premature infant, whose blood prothrombin level and all blood mechanisms are relatively unstable. It is therefore recommended that synthetic vitamin K be given as a routine procedure during labor. Best results are obtained by giving vitamin K within two hours before birth. However, no matter when given during the latter part of labor, definite results are obtained. The dosage is recognized to be 32 mg given intramuscularly. If synthetic vitamin K has not been given to the mother during labor, then it should be administered to the infant immediately after birth. The dosage is also 32 mg, given intramuscularly.

The committee recognizes the multiplicity of problems arising in the care of the premature infant and cannot attempt to answer all of them. The foregoing is included for what value it may prove in the handling of some future case. Two facts are certain in considering care of the premature infant: first, that special care and attention must be provided and, secondly, that time cannot be wasted in applying the best and most recognized treatment procedures.

The infant mortality rates per 1000 live births by years are as follows:

YEAR	RATE
1935	54
1936	4
1937	48
1938	48
1939	45
1940	32

#### STILLBIRTHS

One hundred and eighty-seven stillbirths were reported in 1940, a figure that compares with 211 in 1939. Questionnaires were sent to all physicians reporting still births, and answers were received for 149 cases.

The causes of stillbirths were tabulated as follows:

CAUSE	NO OF CASES
Prematurity	29
Congenital deformity	27
Cause unknown	24
Instrumental delivery	17
Other causes (var ed)	17
Toxemia of pregnancy	16
Hemorrhage (placenta previa or premature separation)	11
Prolapsed cord	4
Syphilis	3
Cerebral hemorrhage	1
	<hr/> 149

Twenty-nine infants were stillborn owing to prematurity, and 27 had some congenital malformation; in 1939, the corresponding figures were 46 and 15. The latter cause is of course unpredictable and unpreventable, whereas premature deliveries might be preventable in the light of recent medical practices involving careful prenatal supervision.

If one studies the foregoing tables on causes of death in infants under one year of age and on stillbirths, the total number of infants lost because of premature births was 130.

There seems to be no conclusion that can be drawn from the number of stillbirths reported during the past few years as shown by the following table:

YEAR	NO OF CASES
1937	181
1938	143
1939	211
1940	187

#### COMMENTS AND RECOMMENDATIONS

As in the past the committee has prepared certain comments and recommendations based on the study carried out. Some definite problems have presented themselves as a result of this year's study. It will be noted that toxemias of pregnancy present a real problem, especially so far as treatment is concerned. Because of continued confusion as to the treatment of toxemia or lack of knowledge as to any type of treatment that might be tried, the committee is including in this report a repetition of the recommendations made in the 1938 report concerning the treatment of toxemia. The committee realizes that no one treatment can be set up as infallible, nevertheless, a simple routine as follows may prove effective:

Absolute quiet.

Sedation (a barbiturate).

Concentrated magnesium sulfate and glucose intravenously (the dose should be regulated according to the needs of the individual case).

Rapid digitalization in all cases with convulsions or threatened with convulsions (for the average patient, a total dose of 20 to 25 gr within twenty-four hours).

The main principles of the treatment consist in sedation, dehydration and, when necessary, cardiac stimulation.

The committee wishes to refer to recommendations made in previous years, with particular reference to indications for cesarean section. A rather comprehensive outline of indications for sections was included in the 1940 report. Other recommendations were that laboratory facilities be used when available for aiding in the diagnosis of conditions that might lead to hazards during delivery; that the proper use of the x-ray in pelvimetry is of value when performed by a competent radiologist; that an *accouchement forcé* done for any condition whatever is condemned; that manual removal of a placenta is unjustifiable unless there is excessive and uncontrollable bleeding; and that more frequent consultations be demanded by hospital staffs for operative deliveries. Recommendations based on the study of 1940 maternal deaths are as follows:

1. Since there have been more deaths from abortions reported for the year 1940, the committee believes that every effort should be made on the part of physicians and authorities to apprehend the offenders and take steps to put a stop to such practices. This recommendation has reference to induced abortions performed without therapeutic indications.

2. The committee considers that too few post-mortem examinations are performed. Any death the cause of which is obscure should be studied in the light of post-mortem findings. It is the belief that most requests for autopsies will be granted if physicians make an effort to secure permissions. Post-mortem vaginal examinations can always be done and may reveal the cause of death.

3. The committee suggests that, in areas where such a procedure is possible, physicians who abhor doing obstetrics and who have no interest in its practice be urged to refer such cases to an obstetrician or to a physician whose chief interest is obstetrics.

4. More care should be exercised in making diagnoses of conditions arising in the prenatal and post-partum periods and of conditions occurring at the time of delivery. Diagnoses appearing on death certificates indicate, in some cases, the failure or lack of effort in coming to definite conclusions. Laboratory facilities, x-rays and careful examinations should be utilized in all cases.

5. Since the use of the sulfanilamide group of drugs has been increased, and since its successful use is dependent on proper dosage, the committee recommends that hospitals make the technics and the tests for blood concentration of these drugs available for physicians' use. To be effective the concentration of sulfanilamide in the blood should be brought up to 10 mg. per 100 cc. and maintained at that level. If the dose prescribed does not attain this end, it is in all probability not adequate. For sulfathiazole the blood concentration should be brought to 3.0 or 3.5 mg. per 100 cc. and maintained at that level.

6. The committee wishes to repeat that there is a tendency on the part of physicians to allow toxemias to continue too long without treatment. A persistent elevation of blood pressure over the known normal for the patient should be considered indicative of toxemia, even without the appearance of albumin in the urine. It is safer to consider that a patient has a mild toxemia until proved otherwise than to ignore it. Abnormal gains in weight should always be viewed with suspicion.

7. The committee recommends that patients be continually urged to seek prenatal supervision. Proper prenatal care should include visits of at least once monthly for the first seven months, and thereafter twice monthly. More frequent visits should be advised during the last trimester if indicated. Prenatal care should include a complete history and physical examination, including a Wassermann test at the outset and follow-up blood-pressure readings, urinalyses, hemoglobin determinations and blood examinations at monthly intervals. Careful records of weight should be kept.

8. Physicians should be discouraged in attempting to perform operative deliveries in the home.

9. Attempts to perform versions without deep anesthesia should be frowned on.

10. It is recommended that physicians keep practical records on all obstetric patients for whose care they are responsible.

11. The committee believes that the physician should make out the hospital record rather than to depend on nurses to do it for him.

12. Whether a delivery is in the hospital or home, the physician should not leave until he is certain the mother's condition and that of the baby are satisfactory.

13. The committee has observed that, in several cases reported this year, sudden deaths occurred on the first day the patients were allowed out of bed. In each case there had been a rise in temperature during the puerperium. It is believed that in cases in which the temperature becomes elevated the possibility of a pelvic thrombosis should be considered and that the patient should be kept in bed until the temperature has remained normal for at least three days. Emboli are common in cases of pelvic thrombosis.

Finally, the committee is most grateful for the excellent co-operation shown this year by physicians. The returns on questionnaires were especially helpful. The frank and complete comments made on many cases were most appreciated. Continued co-operation, interest and further suggestions for this study are earnestly solicited. The committee also expresses its thanks and appreciation to the hospitals that have helped make this study possible. To the Division of Maternal and Child Health of the State Board of Health, the committee expresses its appreciation for the facilities of the division and for the work performed in helping to prepare this report.

ROBERT O. BLOOD, *Chairman*  
BENJAMIN P. BURPEE  
MARION FAIRFIELD

After commending the committee for its excellent work, Dr. D. G. Smith, of the Committee on Officers' Reports, recommended the adoption of the report and the mailing of a copy to each hospital and physician in the State; it was so voted.

The report of the Committee on Child Health was then presented.

### *Report of the Committee on Child Health*

Your committee held five meetings during the year. There was considerable discussion at our meetings of the law making compulsory the reporting of children

with impaired hearing. The State Board of Health asked our advice regarding the formulation of rules and regulations for the proper execution of the law.

The committee has continued to follow as closely as possible progress in child health work, especially as exemplified by the American Academy of Pediatrics. We have continued in close co-operation with the Division of Maternal and Child Health.

At the suggestion of the committee, Dr. Franklin Rogers delivered a radio broadcast on the preschool child over Station WFEA. This has also appeared in *New Hampshire Health News*.

COLIN C STEWART  
TRAVIS P BURROUGHS  
FRANKLIN N ROGERS

The report was accepted.

Dr. Henry H. Amsden read the report of the neurologist.

### Report of the Neurologist

The following deaths have occurred since the last annual meeting.

NAME	ADDRESS	DATE DECEASED
Ballard, Clarence P	Penncook	March 4, 1941
Bartlett, Walter A	Manchester	August 12, 1940
Beaton, Alexander A	Franklin	August 22, 1940
Burt, Edward D	Lincoln	December 2, 1940
Clow, Fred E	Wolfeboro	January 4, 1941
Gilman, Louis L	Rochester	April 11, 1940
Goldsmith, Chester L	Winchester	July 26, 1940
Hubbard, Osmon H	Keene	January 5, 1941
Huse, Ernest L	Meriden	December 21, 1940
Mackenzie, Nicholas Y B	Andover	November 27, 1940
Marks, Homer H	Berlin	April 11, 1941
Morrill, Sibley G	Concord	December 28, 1940
Pherson, Frank J	Manchester	August 27, 1940
Sheldon, Harold L	Troy	September 24, 1940

HENRY H AMSDEN

As matters of new business, Drs. Joseph J. Cobb, of Berlin, Alfred Daudelin, of Nashua, Frank S. Lovering, of Moultonborough, Allen P. Richmond, formerly of Dover, and Lewis G. Hildreth, of Marlboro, were made affiliate members of the Society.

Dr. Wilkins spoke in favor of a change in the by laws whereby one dollar from the dues of each member would be contributed to the Benevolence Fund, rather than fifty cents; he made a motion to this effect, which was seconded and laid over until the following day.

Dr. D. G. Smith moved that the Advisory Committee on Medical Relief be discharged and that its duty be transferred to the Committee on Medical Economics; it was so voted. He then read a letter from the Commissioner of Public Welfare requesting the approval of Dr. L. Theodore Togus's acceptance of his appointment as a member of the

Medical Advisory Committee on Eye Conditions; he moved approval, and it was so voted.

The first meeting of the House of Delegates was adjourned at 11:00 p. m.

\* \* \*

The House of Delegates convened at the Hotel Carpenter, Manchester, on May 13, 1941, at 8:30 a. m., with Vice Speaker Timothy F. Rock, of Nashua, presiding.

The following members answered the roll call.

The President, *ex officio*  
The Secretary-Treasurer, *ex officio*  
Norris H. Robertson, Keene  
Leslie K. Scammon, Hanover  
Frederic P. Lord, Hanover (alternate for Willard A. Bates, Littleton)  
Deering G. Smith, Nashua  
Henry O. Smith, Hudson (alternate for Charles H. Cutler, Peterboro)  
Clarence E. Dunbar, Manchester  
George V. Fiske, Manchester  
George C. Wilkins, Manchester (alternate for Luther A. March, Nashua)  
Charles H. Parsons, Concord  
Herbert B. Messinger, Franklin (alternate for Robert J. Graves, Concord)  
Martha I. Boger-Shattuck, Portsmouth  
Frederick S. Gray, Portsmouth  
Anthony Peters, Portsmouth (alternate for James S. Sanders, Rye)  
Edna Walch, Dover  
Henry C. Sanders, Jr., Claremont

Dr. D. G. Smith, for the Committee on Officers' Reports, moved the acceptance of the first set of changes in the by laws proposed on the previous day and the abolishment of the Committee on Maternity and Infancy, after some discussion it was so voted. He then moved the adoption of the change raising the annual contribution to the Benevolence Fund from the dues of each member from fifty cents to one dollar; it was so voted.

A letter relative to the need of more medical officers for the Reserve Corps and for active duty was discussed.

The second meeting of the House of Delegates was adjourned at 9:15 a. m.

\* \* \*

The House of Delegates convened at the Hotel Carpenter, Manchester, on May 14, 1941, at 8:30 a. m., Vice Speaker Rock presiding.

The following members answered the roll call.

The President, *ex officio*  
The Secretary-Treasurer, *ex officio*  
Clarence O. Coburn, Manchester (alternate for Richard W. Robinson, Laconia)  
Francis J. C. Dube, Center Ossipee  
Frederic P. Lord, Hanover (alternate for Willard A. Bates, Littleton)  
Deering G. Smith, Nashua  
Henry O. Smith, Hudson (alternate for Charles H. Cutler, Peterboro)

Clarence E. Dunbar, Manchester  
 George V. Fiske, Manchester  
 George C. Wilkins, Manchester (alternate for Luther A. March, Nashua)  
 Frederick S. Gray, Portsmouth  
 Anthony Peters, Portsmouth (alternate for James Sanders, Rye)  
 Edna Walck, Dover  
 Albert E. Barcomb, Rochester

Dr. Lord reported for the Committee on Nominations as follows:

#### OFFICERS

*President:* Charles H. Dolloff.  
*Vice-President:* Henry C. Sanders, Jr.  
*Secretary-Treasurer:* Carleton R. Metcalf.  
*Councilors* (five-year term): Cleon W. Colby, John A. Hunter.  
*Trustee* (three-year term): Samuel T. Ladd.  
*House of Delegates:* speaker, Timothy F. Rock; vice-speaker, Charles H. Parsons.  
*Delegate* (American Medical Association): Deering G. Smith.  
*Alternate Delegate* (American Medical Association): Emery M. Fitch.  
*Necrologist:* Henry H. Amsden.

#### STANDING COMMITTEES

*Amendments to Constitution and By-Laws:* James B. Woodman, Frederick S. Gray, W. J. Paul Dye.  
*Child Health:* Colin C. Stewart, Jr., Travis P. Burroughs, Franklin N. Rogers.  
*Control of Cancer:* George C. Wilkins, Howard N. Kingsford, George F. Dwinell.  
*Maternity and Infancy:* Robert O. Blood, Benjamin P. Burpee, Marion Fairfield.  
*Medical Economics* (three-year term): Richard W. Robinson.  
*Medical Education and Hospitals:* John P. Bowler, James W. Jameson, Herbert L. Taylor.  
*Mental and Social Hygiene:* Charles H. Dolloff, Benjamin W. Baker, John B. McKenna.  
*Public Health:* Chester L. Smart, Harris E. Powers, Anthony E. Peters.  
*Public Relations:* Charles H. Dolloff, Henry C. Sanders, Jr., Carleton R. Metcalf, Robert J. Graves, Joseph N. Friborg.  
*Publication:* Carleton R. Metcalf, Warren H. Butterfield, Ellsworth M. Tracy.  
*Scientific Work:* Carleton R. Metcalf, Frederick P. Scribner, Nathan T. Milliken.  
*Tuberculosis:* Robert B. Kerr, Robert M. Deming, M. Dawson Tyson.

The report was accepted. The Secretary was instructed to cast one vote for Dr. Dolloff as president; this was done, and he was declared duly elected.

Dr. J. J. Morin, of Rochester, and Dr. H. L. Taylor, of Portsmouth, were nominated for the office of vice-president, in addition to Dr. H. C. Sanders, Jr. Following written ballots, it was announced that Dr. Sanders had received 13 votes, and Dr. Morin, 1; Dr. Sanders was declared duly elected.

The Secretary was instructed to cast one ballot for Dr. Metcalf as secretary-treasurer, and one for the remainder of the officers and committee members as nominated; this was done, and all were declared duly elected.

Dr. Coburn moved that the Society, through the House of Delegates, extend a vote of thanks to Dr. H. O. Smith for his work in bringing the history of the New Hampshire Medical Society to date and compliment him on his efforts as chairman of the committee in charge of the one hundred and fiftieth anniversary; it was so voted. He then moved that a vote of appreciation and thanks be extended to the committee that had had charge of arranging the very interesting and popular medical exhibit; it was so voted.

Dr. Metcalf moved that a vote of gratitude be extended to the members in Manchester who had arranged the details of the meeting; it was so voted.

Dr. Wilkins raised the question whether certain moneys from the General Fund should be transferred to the Benevolence Fund, thus providing a small income that could be used for needy cases. After some discussion, it was voted that the trustees be given power to expend money from the General Fund for the relief of needy members.

After some discussion, it was the consensus that a social gathering similar to the one held on the previous evening be held for the next two or three years.

It was further decided that the 1942 meeting be held in Manchester.

Dr. Wilkins moved that a vote of thanks be extended to Dr. George Dwinell for his work in scheduling and arranging the commercial exhibits during the previous six or seven years; it was so voted.

Dr. H. O. Smith called attention to the fact that the badge being used by the members of the Society was a replica of one presented to the members in 1906 by the president, Dr. F. A. Stillings;

at that time it was voted that the button be made a permanent badge, but the vote was forgotten three years later. He also said that at one time the Society had had a valuable reference library, its nucleus being the gifts of Dr Joshua Brackett and his widow. In 1891, there were over three

hundred volumes at Dr Irving A. Watson's office at the State House, however, no trace of these books can be found.

The third and final meeting of the House of Delegates was adjourned at 9:25 a.m.

CARLETON R. METCALF, *Secretary*

## MEDICAL PROGRESS

### THE TREATMENT OF DEHYDRATION IN PATIENTS WITH HYPERTROPHY OF THE PROSTATE, RETENTION OF URINE AND IMPAIRMENT OF RENAL FUNCTION\*

F. A. SIMEONE, M.D.

BOSTON

OF recent years, the problem presented by hypertrophy of the prostate and the interference with the normal function of the urinary organs caused thereby has been discussed in the literature largely by articles dealing with the technic of prostatectomy, whether by the transurethral, transvesical or perineal routes, and with analyses of end results of such operations. Discussions of measures to improve the badly disorganized general condition shown by many such patients, so that they may survive any form of operation have been less numerous. It is nevertheless essential to point out that the gratifying reduction of both mortality and morbidity of earlier years was the result of improvements in the preoperative and postoperative conduct of the patients rather than of improvements in operative technic, however valuable these may have been. The removal of the prostate in two stages resulted from a realization of the necessity for restoring the patient's disordered metabolic and chemical processes to a condition as nearly normal as possible before subjecting him to prostatectomy. Thus, in 1914, Pilcher<sup>1</sup> stated:

The chief indication is primarily to relieve the retention of urine rather than the removal of the prostate. If we could dissuade surgeons, as a rule, from the course of immediately taking out a prostate which is known to be obstructive, we would do much to help the cause of the prostatites.

The cardiovascular and the renal excretory systems bear the brunt of the secondary effects of prostatic hypertrophy. In patients of the age group in which hypertrophy of the prostate occurs, the heart and circulation are often already the seat of natural changes that decrease, some times practically to annihilation, the reserve that these systems possess in men of younger age groups. When obstruction to the outflow of urine from the kidneys occurs, the burden of an increased arterial blood pressure is added to the already overtaxed heart. When such elevation of blood pressure has existed for a long time, a rapid fall of blood pressure following decompression of the urinary passages, such as that afforded by catheterization, may induce profound changes in the blood flow through vital organs. Certain cases of disorientation, coronary occlusion and oliguria or anuria after too rapid decompression of the obstructed bladder may be referable to such circulatory changes. The treatment of the failing heart and circulation thus assumes a major role in the management of patients with prostatic hypertrophy of long standing.

The secondary effects of the obstructing prostate on the renal excretory system itself are referable principally to infection and to derangement of renal function. The burden that infection places on the bodily economy needs no emphasis. The service that chemotherapy, particularly the use of sulfanilamide and sulfathiazole,<sup>2,3</sup> has rendered to those suffering from infection in the urinary tract is now generally recognized. The fact that these drugs act in especially small

\*All articles in this series will be published in book form the current volume is *Medical Progress Annual 1940* (Springfield Ill no. 8 Charles C. Thomas Company 1941 \$4.00).

<sup>1</sup>From the Urology, and Clinic, Peter Bent Brigham Hospital.  
<sup>2</sup>Instructor in general urinary surgery Harvard Medical School fellow urology Peter Bent Brigham Hospital.

amounts in urinary infection is particularly fortunate. To be sure, they are not curative in the presence of obstructing lesions of the urinary tract, but this does not detract from their value as adjuncts to bladder drainage in preparing patients with urinary retention and infection for prostatectomy.

Among the widespread effects of renal insufficiency accompanying prolonged urinary obstruction, the most serious from the point of view of the urologic surgeon is the derangement in water balance and in the electrolyte pattern of the body fluids. Clinically, interest centers on the treatment of the dehydration that almost invariably attends the deranged electrolyte composition of the body fluids. The importance of water and electrolytes for the proper execution of body functions cannot be overemphasized. The maintenance of normal metabolic reactions, as well as such complex functions as wound healing, depends on a proper complement of water and electrolytes. A brief summary of the problems encountered in the management of water balance or dehydration in urologic patients is therefore profitable.

The proper management of dehydration depends on three premises: recognition of the state of dehydration, detection of the underlying causes and familiarity with methods available for correcting the condition.

#### THE DIAGNOSIS OF DEHYDRATION

The clinical signs of dehydration are easy to recognize. The skin is warm, dry, wrinkled and inelastic. The eyeballs are soft. The tongue is dry and difficult of motor control so that speech is thick. If dehydration is sufficiently severe, acetone may be detected on the breath. The sensorium is dulled in varying degrees up to coma. The pulse is rapid, but the arterial blood pressure may be normal until the condition is far advanced, when a state resembling secondary shock supervenes. Acidosis is usually present, with its attendant respiratory changes, but there may rarely be alkalosis, even when ketone bodies are being excreted in the urine.

Such clinical signs as have been described, however, usually accompany a loss of 6 per cent or more of the body weight in water. Slight degrees of dehydration are often difficult to recognize. To detect dehydration before too serious metabolic disturbances have been created, several laboratory tests have been employed. The commoner ones are the following.

*Red-cell count and hematocrit determination.* An increase in the number of red cells in the blood stream, as determined by red-cell counts and hematocrit determinations, has been interpreted as indicating a decreased content of water in the blood (anhydremia) and, indirectly, a decrease in the volume of interstitial fluid (dehydration). Such an interpretation is justified in the absence of primary or secondary polycythemia from other causes, such as cardiopulmonary disease. The findings, however, are not always dependable. The tests may be normal when the dehydration is slight, because of the efficiency of the homeostatic mechanisms in maintaining constancy in the blood by drawing on the fluid stores in the interstitial (subcutaneous) tissues. When dehydration has been severe and of long standing, anemia develops secondary to destruction, as well as to depressed formation, of red blood cells. A normal or subnormal red-cell count and hematocrit determination may thus be misleading.

*Specific gravity of the blood and serum-protein concentration.* These tests are as easily done as the red-cell count and the hematocrit determination.<sup>4, 5</sup> They are subject to the same faults, however. Considerable interstitial fluid may be lost before any marked change becomes apparent in the concentration of the serum or plasma protein. On the other hand, one may encounter normal plasma-protein concentrations or actual hypoproteinemia in severe chronic dehydration because of the destruction of blood proteins when anhydremia is prolonged.

*Study of the electrolyte pattern of the blood plasma.* Here again the numerous reactions that maintain stability within the circulating fluids militate against early detection of dehydration until the condition has advanced so far that the homeostatic mechanisms begin to fail. At this point, one almost always finds a depression in the total-base component of the blood plasma, represented largely by sodium. The base depletion, by conditioning an equivalent loss of water, may be a primary cause for the dehydration (as in patients with biliary, pancreatic and intestinal fistulas), or it may be a secondary effect of prolonged or severe dehydration that has caused an impairment of renal function. In fact, so long as there is normal renal function,—or perhaps more accurately, so long as there is opportunity for normal renal function,—the total base of the blood plasma remains normal, even in the presence of moderately severe dehydration.

The value of estimating the electrolyte pattern of the blood lies in the information derived therefrom concerning the *degree* of derangement present and the approach suggested thereby for fluid replacement therapy.

*Estimation of the fluid need of interstitial tissue.* Hopps and Christopher<sup>6</sup> adapted the intradermal wheal absorption test of Aldrich and McClure to the study of dehydration in surgical patients. The test consists in the intradermal injection of 0.2 cc. of physiologic saline solution to raise a wheal, whose rate of disappearance is then measured. Normally, such a wheal disappears in fifty five or more minutes. A decreased disappearance time indicates a scarcity of subcutaneous fluid, or dehydration. Actually, however, the test probably reflects the existing osmotic conditions in the skin and subcutaneous tissues and not necessarily the lack of body water. Thus Kunde<sup>7</sup> found that the disappearance time decreased in cases of hydropigenous nephritis. In fact, it was possible to detect a decrease in the disappearance time even before the appearance of edema. Cases exhibiting edema, however, may still present the picture of dehydration in the broad sense of the term. Cases in which the total content of body water is normal or actually greater than normal might more properly be considered to represent disordered distribution of body water rather than dehydration.

It becomes apparent that slight changes in the concentration of plasma constituents, which may be sufficient to call into action the numerous regulatory mechanisms that preserve constancy while dehydration is progressing, cannot be detected by the usual analytical methods. Determinations of blood volume are not applicable to the study and treatment of early clinical dehydration. Evaluation of the Aldrich-McClure intradermal wheal absorption test must wait until more experience has been had with the test. The activity of the salivary glands, however, is a sensitive indicator of the state of hydration of the body. Long before ionic changes are demonstrable in the blood, the withdrawal of interstitial fluid causes a diminution in the blood flow through the salivary glands, the secretions from which are thereupon impoverished. Thus, the best index of early dehydration is the old clinical observation of dryness of the buccal and oral mucous membranes. Dysphagia is frequently present and may appear early in patients suffering from prostatism. Since dehydration may actually be secondary to hyposthenuria, the excretion of normal, or greater than nor-

mal, volumes of dilute urine is not inconsistent with dehydration.

The value of blood chemical determinations is not to be belittled, however. They at least demonstrate the degree of dehydration, and the nature of the shift in electrolyte pattern serves as a guide for replacement therapy.

#### ETIOLOGIC FACTORS IN DEHYDRATION

For convenience of description, the causes of dehydration fall into two major groups: those in which deficiency of fluid in the body results either from lack of fluid intake or from loss of water and salts through wastage of body secretions, and those in which water is lost secondarily because of disturbances in the electrolyte composition of body fluids due to abnormal function of the kidneys. Dehydration secondary to hemorrhage or loss of plasma through denuded skin surfaces, as in severe burns, is a special case that belongs to the first category. The treatment of the dehydration encountered in the first group has been discussed in several publications (Maes and Davis<sup>8</sup>). The second group of cases, which are of special interest to the urologist, however, have received little attention. The frequency with which patients with urinary retention and impaired renal function exhibit a dehydration that is practically always secondary to a multiplicity of factors warrants further analysis of the nature of dehydration in patients with hypertrophy of the prostate, urinary retention and renal insufficiency.

The principal factors determining dehydration in such urologic patients are insufficient fluid intake, loss of water and salts from the body and electrolyte imbalance due to impairment of renal function, with consequent loss of body water.

*Insufficient fluid intake.* Metabolic activity involves a daily inevitable loss of water from the body. The greatest volume is lost by vaporization from the skin and lungs. The actual amount lost naturally varies with body temperature, muscular activity and the temperature and humidity of the environment. On the average, however, 2000 cc. a day are lost by vaporization. Next in amount is the water lost through the kidneys in the form of urine. So long as renal function is normal, the water excreted by this route varies inversely with the amount of water lost through other channels. When the water stores in the body are low, the normal kidney conserves water by excreting a concentrated urine. The diseased kidney, however, is unable to extract water efficiently from the glomerular filtrate, and water is wasted. Thus, the normal kidney can excrete an average of 35 gm

of solids in little more than 400 cc. of urine. The diseased kidney, which is unable to concentrate beyond a specific gravity of 1.010, requires 1500 cc. to excrete the same amount of solids. Normally, the water lost in the stools is negligible.

For metabolism to proceed normally, this inevitable daily loss of body water, amounting to about 3500 cc., must be replaced, and this is accomplished by the ingestion of water with food or drink regulated by the sensation of thirst. The metabolic water derived from the breakdown and transformation of food elements seldom amounts to more than 500 cc., and in patients who have limited their food intake because of illness, water derived from this source is negligible. It is noteworthy that patients with urinary retention, renal insufficiency and nitrogen retention often are not thirsty, even though they present obvious clinical signs of dehydration. They sometimes actually complain that water "tastes bad" and refuse to drink. A vicious circle is thus established whereby dehydration, which may have begun by electrolyte derangement, is aggravated by inadequate fluid intake.

*Loss of body fluid through abnormal channels.* In addition to loss of water in the urine and by vaporization, which, except in degree, does not differ from the normal, fluid may be lost by various abnormal means. These are common knowledge, and the problems presented by such avenues of fluid loss as biliary and intestinal fistulas are not germane to the consideration of dehydration in the prostatic patient with renal insufficiency and nitrogen retention. The urologist is often confronted, however, with the necessity of replacing fluid lost by vomiting and sometimes by diarrhea. It should be pointed out here that vomiting in such patients is not prone to cause alkalosis but rather dehydration and acidosis because of the relative achlorhydria in azotemia. What chloride escapes in the vomitus does so in company with sodium.

*Loss of body fluid because of changes in the electrolyte pattern of the blood secondary to impairment of renal function.* Changes in the electrolyte composition of the blood associated with impaired renal function are varied. Irrespective of the type of renal disease, however, the principal changes are referable to the total base (principally sodium) and the chloride and bicarbonate acid ions.

The determination of the total-base equivalence of blood plasma offers an accurate index of its osmotic characteristics, which depend in large measure on the electrolyte content of the plasma. The total-base concentration in the plasma of patients

with renal insufficiency is almost invariably low. The mechanism whereby salt is spared by the kidney is lost. Water is lost along with the base, and dehydration ensues. It is only with far advanced total-base depletion and disordered renal function that water is retained in spite of low total-base concentration in the blood and tissue fluids.

The mechanism for base depletion in renal disease is not entirely clear, but an important role is no doubt played by the inability of the diseased kidney to synthesize ammonia, with which to excrete nonvolatile acids as ammonium salts. Instead, they are excreted as salts of fixed base derived from the blood plasma.

In renal disease, the concentration of the chloride ion in the blood is very variable. Thus in 148 cases of varied etiology, Peters, Wakeman, Eisenman and Lee<sup>9</sup> found that the chloride determinations were below normal limits in 56, and above in 44. A low blood-chloride concentration, however, does indicate almost invariably a low total-base or total-electrolyte concentration in the blood, with consequent loss of water in the attempt of adjustive mechanisms to restore osmotic equilibrium. A low total base, however, does not necessarily imply a low chloride concentration. The usually reciprocal relation between the concentrations of the chloride and bicarbonate ions prevents the loss of chloride when the total base concentration has become low, that is, the bicarbonate ion variation is the principal mechanism whereby a balance is maintained between the acid and base equivalence of the blood electrolytes. Hence, acidosis usually accompanies dehydration, and base is lost from the blood without a corresponding loss of chloride.

Even in dehydration secondary to electrolyte imbalance, the very causation of the dehydration makes impossible its early detection by chemical study of the blood plasma. Changes in the electrolyte pattern of the blood are detectable by gross methods only when the causative factors have progressed to such degree that compensation for them by the usual homeostatic mechanisms has begun to fail.

#### TREATMENT OF DEHYDRATION

In the management of the postoperative patient with urinary retention and impairment of renal function, the administration of 3500 cc. of fluid every twenty-four hours is sufficient to replace the inevitable fluid loss from the body during convalescence. It ensures the availability of about 1500 cc. of water for excretion in the urine, and this is sufficient for the excretion of 35 gm. of solids even by kidneys that cannot concentrate beyond



a specific gravity of 1.010. Fluid lost through vomitus or other abnormal channels must be measured and replaced in the form of physiologic saline and dextrose solution, in addition to the 3500 cc. When the function of the kidneys is normal, it makes little difference in what form the inevitable fluid loss from the body is replaced, provided that 8 to 10 gm. of salt per day is furnished. Fluid lost through acute hemorrhage is, of course, best replaced by whole blood, and the protein-rich fluid lost in exudates, by blood plasma or serum.

The treatment of dehydration in the presence of primary or secondary electrolyte imbalance requires special consideration. The choice of the various types of fluids available for parenteral therapy depends on the nature and degree of the electrolyte imbalance, and the success of therapy depends in part on the choice of proper fluids and in part on the degree to which renal function can be restored. It is essential to remember that each case of dehydration with disturbed blood-electrolyte composition presents problems peculiar to itself, and that treatment must therefore be individualized. Nevertheless, certain general principles may be formulated.

*Cases in which dehydration is mild and renal function is normal.* These cases are seldom of any concern. The dehydration is usually secondary to insufficient fluid intake because of the associated illness. Fluid loss through abnormal channels plays only a small part, if any. Therapy is simple. According to the degree of dehydration, as estimated clinically, 1000 to 2000 cc. of fluid are administered parenterally, in addition to the 3500-cc. requirement for the twenty-four hours.

*Cases in which dehydration is severe but renal function is adequate.* These patients have experienced water deprivation for longer periods or have lost large quantities of fluid by vomitus, diarrhea or fistulas. The principles of parenteral fluid therapy are the same as those for the preceding group, but larger volumes of fluid are required. Such patients may have lost as much as 6 per cent or more of their body weight in water, and this must be replaced in addition to the basic requirement of 3500 cc. It is not uncommon, therefore, for a patient who is severely dehydrated to require 7000 cc. or more of fluid in twenty-four hours. Most of this may be given in the form of 5 per cent dextrose in distilled water, but enough of it must be in the form of physiologic saline to provide a daily minimum of 8 or 10 gm. of sodium chloride and to replace fluid lost through vomiting and diarrhea, volume for volume.

Acute severe dehydration of short duration is accompanied by the signs of hemoconcentration

described above. In such cases, care must be taken to avoid too rapid administration of fluid to obviate overloading the heart by sudden dilution of the blood, which might otherwise ensue. It may thus require as long as ten or twelve hours to administer the full complement of fluid for twenty-four hours in a severely dehydrated patient. It must be emphasized that when dehydration has been of long standing, or when for other reasons the anhydremia is accompanied by loss of plasma protein and red blood cells, the blood volume is to be restored, not by means of solutions of crystalloids, but rather by means of whole blood or blood plasma. In such cases, the administration of crystalloid solutions often initiates hypoproteinemia, not only by dilution of the blood but also by actual loss of protein from the capillary bed.

*Cases in which dehydration and impaired renal function coexist.* Severe dehydration is known to have profound effects on both the structure and the function of the kidneys. Thus, red blood cells, casts and albumin are not uncommonly found in the urinary sediment of such patients. In addition, there is often nitrogen retention of considerable magnitude in the blood. Yet, when the renal effects are secondary to dehydration resulting from other causes, the treatment is hardly more difficult than that described for the last group above. Renal function is usually promptly restored by the administration of fluid in the form of dextrose solution. This has special value in combating the ketosis and acidosis that such patients often exhibit. Not only are water and carbohydrate thereby supplied to restore to normal the metabolism of the ketogenic substances, but proteins are spared from catabolism so that the necessity for eliminating nitrogenous products and nonvolatile acids is decreased.

The cases of dehydration due to or complicated by chronic disease of the kidneys are the most difficult to treat. It is in this group that patients with hypertrophy of the prostate and urinary retention fall. Study of these cases makes one realize the important work the kidneys perform in regulating the pattern of osmotically active ions in the blood.

The first consideration in the treatment of such patients is restoration of the blood volume to as nearly normal as possible. Unlike the cases in the two groups described above, these patients usually show no laboratory evidence of hemoconcentration. The red-cell count, the hematocrit and the specific gravity of the blood may be quite normal. Yet the skin and mucous membranes are dry, there may be acetone on the breath and in the urine, and study of the blood electrolytes may show base depletion and acidosis. While prepara-

tions are being made for relieving the urinary obstruction, therefore, these patients should receive 500 cc. or more of blood plasma, or of whole blood if there is anemia or if plasma is not available. Further restoration of fluid balance is accomplished by the administration of crystalloid solutions, and the choice of fluid depends in large measure on the characteristics of the blood electrolyte disturbance.

In contrast to the almost invariable finding of a lowered total-base concentration in the plasma of patients with dehydration and renal insufficiency, the concentration of the chloride ions may be increased to well above its normal value. This, of course, implies a drop in the concentration of the bicarbonate ions and a lowering of the alkali reserve. After the blood volume has been restored by transfusion, the next step is to induce a diuresis by the slow injection of glucose solution (1000 cc.) followed by glucose in physiologic saline solution. These solutions are alternated until the total desired volume for the twenty-four-hour period has been attained. The objection to using dextrose solution alone is that the very production of diuresis in hyposthenuric kidneys causes salt wastage and further depletion of base. Furthermore, it appears impossible for such kidneys to excrete chloride and retain base. Acidosis thus persists in spite of saline infusions, and when the diminution in alkali reserve has become sufficiently severe, these form the ideal cases for the administration of sodium bicarbonate or of sodium lactate (Hartmann-Senn solution) intravenously.

Not infrequently, the depletion of total base is accompanied by loss of chloride. When the chloride concentration of the blood is sufficiently low, the bicarbonate concentration may be quite normal. The mechanism of the decreased blood chloride is often difficult to explain. Even when there has been considerable vomiting, the cause for the hypochloremia remains obscure, since patients with even slight nitrogen retention in the blood are apt to have moderate to complete achlorhydria. As in the cases with chloride retention, the first indication is to restore the blood volume by means of whole-blood or plasma transfusion. The electrolyte concentration can then be brought to normal by the administration of glucose in physiologic saline solution. Some advocate the administration of Ringer's solution in place of sodium chloride solution. The advantages of the more complex fluid are only slight. It is in this group of cases that, owing to renal insufficiency, it is easily possible to effect a higher than normal electrolyte concentration in the blood, with consequent plethora and edema. Blood-chloride con-

centrations should therefore be checked at frequent intervals. The unregulated use of dextrose solution, however, can lead to equally distressing complications. The diuresis incident thereto washes base from the blood and leads to further depletion, and in addition there is actual loss of protein from the blood stream.

These urologic problems in dehydration are frequently complicated further by heart failure and peripheral edema. The same general principles outlined above still hold. The choice of fluids is based on the same principles, but the administration should be slower and the total volume of fluid should be curtailed until cardiac compensation has been restored. When diuresis begins, however, as a result of cardiac improvement due to bedrest or digitalis, fluids should be urged rather than restricted, to avoid the concentration of waste products in the tissue fluid and blood (uremia), which may result when the kidneys are unable to concentrate urine beyond the specific gravity of 1.010.

The preceding discussion has implied that fluid replacement therapy is accomplished entirely by vein. But fluid may be administered subcutaneously as well as intravenously when there is no peripheral edema. It is customary to use 4 rather than 5 per cent solutions of dextrose for subcutaneous injection. The injection of more than 2000 to 2500 cc. a day by the subcutaneous route, however, is seldom necessary. When co-operation is possible on the part of the patient, the fluid intake by mouth may be supplemented by the rectal administration of tap water, glucose solution or physiologic saline solution.

Finally, it should be emphasized that the best method of administering fluid is to encourage the patient to take it by mouth whenever possible. To overload the stomach in an effort to avoid parenteral administration of fluid, however, is a sad commentary on clinical judgment.

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CASE RECORDS OF THE  
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

## CASE 27341

## PRESENTATION OF CASE

A thirty-four-year-old salesman entered the hospital for study.

Fifteen years before admission, the patient received a blow in his left back and felt something snap in the region of his left scapula. The part was painful on deep breathing, sneezing and coughing for three weeks, and sometime later he noticed a lack of sensation of his left hand when he dipped it in hot or cold water, at a temperature painful to his right hand. In addition an inconsistent, nonradiating, burning pain occasionally appeared in the left anterior or posterior chest, and in the left upper or lower arm. This sensation occurred at irregular intervals, lasted seconds to minutes, and varied in location. The patient visited the Out Patient Department, where a loss in tendon jerks and a decrease in pain and temperature sense were noted in the left arm. He was studied thoroughly, and since no organic cause was found to account for the condition, it was considered to be hysterical in origin. Over the fifteen years prior to admission, there was no appreciable change in the patient's symptoms, although pain sensation returned in some degree to his left hand. Immediately before entry, the patient was subjected to a routine examination for employment, and a mediastinal mass was demonstrated by x-ray film. At no time had there been cough, hemoptysis or weight loss.

Physical examination was entirely negative except for diminished pin and temperature sensations over the left arm and hand; this was too vague in its distribution to be mapped out. All tendon reflexes were absent in the left arm, but present in the right.

The temperature, pulse and respirations were normal.

Examination of the urine and blood was negative. A blood Hinton reaction was negative. Findings on lumbar puncture were normal, and a spinal-fluid Wassermann test was negative.

X-ray films of the chest showed a soft-tissue mass, 7.5 by 6.5 cm., at the posterior aspect of the left chest close to the fifth, sixth and seventh ribs. The fifth rib showed a pressure defect on

its lower border, and the sixth rib was flattened and widened in the region of the mass, the changes in the flattened portion being interpreted as an old, healed fracture. The rest of the chest showed no abnormalities.

An operation was performed.

## DIFFERENTIAL DIAGNOSIS

DR. THEODORE L. BADGER:\* May we see the x-ray films?

DR. AUBREY O. HAMPTON: The lateral views are not here. I think we can accept the interpretation of the size and location of the soft-tissue mass. You can see the upward concavity of the fifth rib, which looks as though it had been pushed up by pressure, and the enlargement of the sixth, with definite alteration in structure; there is no



FIGURE 1.

deformity of the seventh (Fig. 1). Within this mass, there are flocculent areas of calcification, not mentioned in the report.

DR. BADGER: There is no evidence of bone destruction so far as the vertebra is concerned?

DR. HAMPTON: I do not believe so, but the vertebrae are not well seen. The mass is close to the spine. One might expect it to be eroded by pressure just as this rib is. I might say that this appearance in the rib is not by any means typical of a healed fracture.

DR. BADGER: Summarizing the case briefly, we have a man who, following a blow in the left back fifteen years before admission, developed secondary symptoms in the left arm, which have recurred from time to time up to the present, essentially without change in character. In the present illness, these symptoms were fleeting pains that

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came and went in the left arm, loss of tendon jerks, and loss of sensation to cold and heat, symptoms that are almost identical to those noted fifteen years previously. At that time, no definite cause for the neurologic findings was discovered.

Do you know whether an x-ray film was taken at the time of the blow?

DR. RALPH ADAMS: No x-ray film of the chest was taken.

DR. BADGER: The important features really boil down to what was apparently a fracture of the left sixth rib when the patient received the injury. He had pleuritic pain on cough, sneezing and deep breathing, consistent with fracture of a rib. We do not know the severity of the blow. The symptoms and physical findings have not changed in any way. The neurologic findings, which were extremely vague, were the same at the time of the injury as they were at admission. The areas with loss of pin sensation are not accurately demonstrated. No mention is made either of atrophy of the hand or of differences in the two pupils, and Horner's syndrome was apparently not present. Therefore, I am at a loss to know whether this left-arm syndrome is definitely to be connected with the original trouble. Clinically, the patient was well, with no symptoms except in the left arm and hand. He was being examined for a new job. The laboratory findings were entirely negative. Had it not been for the x-ray picture, I gather there would have been no discovery of the underlying pathologic lesion.

This mass shows some calcification in its center, the left sixth rib is definitely abnormal, and there is a pressure distortion of the fifth rib posteriorly. The differential diagnosis in this case revolves around the character of the tumor mass. It seems unlikely that the tumor was malignant, because it would be unusual for a malignant tumor to be present fifteen years without more significant changes, although we might find malignant changes developing late in a primary benign tumor.

But if it was a benign tumor, how are we going to account for it? It occurs to us at the start that a severe blow in the back with considerable pain and with symptoms indicative of fracture might have had something to do with it. We wonder whether this was an unusual hematoma resulting from the fracture, which had never been observed and which had calcified over a period of years without significant change in size. That would to some extent account for the picture presented. There appears to be no definite evidence

of an aneurysm. The signs are not consistent with it. The arch and descending aorta were normal, and the spinal-fluid Wassermann test was negative. Dermoids and teratomas are more likely to be seen in the anterior chest, and I believe they can be ruled out. Lymphosarcoma or Hodgkin's disease was probably not responsible.

If the mass was in any way associated with the symptoms, which persisted for years, we find ourselves reduced to three possibilities. If the mass was associated with the original injury, it should be a benign tumor—either a hematoma or a neoplasm of slow growth. Chondromas are likely to be posterior tumors in the upper portion of the chest and might be related to the bone injury. The x-ray findings were not quite characteristic of chondroma, but I think it could have been that, and the pressure symptoms for a long period of time might in part have been due to such a tumor. We must also bear in mind the possibility of neurofibroma. So far as benign tumors are concerned, neurofibroma is probably a good bet for explaining symptoms over a long period—an entirely benign tumor presenting no symptoms except neurologic ones, explainable on the basis of neurofibromatous involvement of some portion of the nerve roots. If the tumor involved the first, second or third rib, I should be more inclined to account for the neurologic symptoms, on the basis of pressure or invasion, than I am able to in the location where it actually occurred. There appeared to be no involvement of the sympathetic chain, for there is no comment about alterations in the left pupil. Also, there was no apparent atrophy of the left hand. In fact, I am a little confused about the neurologic findings: they were constant so long and yet produced no secondary changes. I am, therefore, inclined to divorce the neurologic findings from the underlying lesion in the chest and to believe that they may be explained on some other basis.

I think that this is a benign tumor, and I name chondroma, calcified hematoma and neurofibroma, in that order, as the most likely possibilities.

DR. DONALD S. KING: I saw this patient once in the Thoracic Clinic. We put neurofibroma first, with secondary changes in the ribs from pressure. Our opinion had been changed at the time the surgeons operated, but that was our original impression.

DR. CHARLES S. KUBIK: Have we ever had a neurofibroma with calcification?

DR. HAMPTON: We have had a ganglioneuroma, with calcification and secondary involvement of the ribs, but not like this. This rib should have

given us more pause. The X-ray Department made a diagnosis of neurofibroma. I do not know whether they changed later or not.

DR. WYMAN RICHARDSON: Do you have to think of vascular tumors—hemangioma and so forth?

DR. HAMPTON: The widened rib and the change in structure should make one suspect a primary bone tumor. It could be a vascular tumor, or an osteochondroma; and we have a few cases of bone changes similar to that in vascular neurofibromas. I do not know how content we should be with any diagnosis, but I think Dr. Badger's reasoning is a little better than ours.

DR. EDWARD D. CHURCHILL: I think we were a little hasty in attributing the changes in the ribs to the pressure of a neurofibroma. A neurofibroma arising from the intercostal nerves gives extreme deformity of the ribs. They look nothing at all like these ribs. They are thin, keel-like structures, completely surrounded by slowly growing tumor. All of us who saw this man made a provisional diagnosis of neurofibroma. I wish Dr. Kubik would tell us just how this tumor is destroying the tendon reflexes in the left hand.

DR. KUBIK: I cannot explain it any more than Dr. Badger could. The tumor is not in the right place to do so, and perhaps one cannot assume it was present for fifteen years, or from the time that the patient first observed neurologic symptoms. It obviously could not have been hysteria if the tendon reflexes were gone. The findings suggest more than one lesion, and therefore favor neurofibroma. There may be another lesion, possibly intraspinal, although the lumbar-puncture and spinal-fluid findings do not suggest that, in fact are rather against it.

DR. HAMPTON: Osteochondromas are also multiple.

DR. KUBIK: I should not have thought of neurofibroma, because of the calcification, which I cannot remember having seen with neurofibroma.

DR. ADAMS: Dr. King's note from the Thoracic Clinic reads, "The x-ray findings are characteristic of neurofibroma with rib changes, but no erosion; Dr. Churchill strongly inclines toward surgery." At operation, the sixth rib was densely adherent posteriorly and grossly deformed by intrinsic tumor. The rest of the tumor was found lying in the costovertebral gutter, with the left sympathetic chain forced backward over its posterior aspect and closely adherent. The tumor stopped abruptly at the head of the rib. The pleura could be separated from its attachments without profuse bleeding. The tumor seemed to be composed of irregular bony fragments, which

felt like a bag of gravel. I thought at that time that the preoperative diagnosis of neurofibroma should be changed to chondroma. The tumor was easily removed, and the patient made an uneventful recovery.

#### CLINICAL DIAGNOSIS

Neurofibroma.

#### DR. BADGER'S DIAGNOSIS

Chondroma of the lung, or  
Calcified hematoma in the region of the posterior end of the sixth left rib, or  
Neurofibroma.

#### ANATOMICAL DIAGNOSIS

Cavernous hemangioma of the left sixth rib.

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: An interesting phenomenon, which was apparent as soon as the tumor was removed, was that the resected specimen was only half the size of the specimen in the body, as judged by the x-ray films. In other words, it had shrunk 50 per cent during resection, and the reason became obvious as soon as we cut across it. It consisted of a great mass of dilated blood vessels, with small spicules of bone between them. Its gross and microscopic appearance was characteristic of a cavernous hemangioma.

DR. HAMPTON: Was there no neurofibromatous tissue in it? It could not be called a vascular neurofibroma?

DR. MALLORY: No.

DR. MAURICE FREMONT-SMITH: Has anything happened to the neurologic symptoms?

A PHYSICIAN: No; we have not yet explained the symptoms in his arm except to guess they were due to the proximity of the tumor to the sympathetic chain.

DR. KUBIK: I do not see how that could be the explanation, but the patient may have had another hemangioma, perhaps a very small intraspinal one, which would not necessarily produce any spinal-fluid changes.

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#### CASE 27342

#### PRESENTATION OF CASE

A fifty-three-year-old housewife was admitted to the hospital in a semicomatose condition.

Two weeks before admission, the patient was taken ill while in Florida with general malaise and fever of 99 to 102°F. Her condition was diagnosed and treated as "grippe," and the pa-

tient apparently improved, since she was able to ride home by automobile three days later, arriving home one week before admission. During the next two days, she felt well enough to do some housework, but four days before admission she again had general malaise and fever of 102°F. The following day, she developed a slight cough and a stiff neck, and her temperature was 101°F. She was seen by her physician, who found nothing on physical examination except a stiff neck. The day before admission, she felt much better, and her temperature remained normal. On the day of admission, fever recurred, reaching 105.6°F. A sputum examination showed large numbers of Type 8 pneumococci. A white-cell count was 19,000 with 84 per cent polymorphonuclears. The patient was given two 15-gr. doses of sulfathiazole, and in the evening, after being seen by a consultant, was given 30 gr. more and then admitted to the hospital.

The patient had had measles, followed by pyelitis, ten years before admission.

Physical examination showed a well-developed and well-nourished, semicomatose woman who was mumbling slightly, with rare coughing spasms, and who resisted being disturbed. The skin was dry, and the pupils were equal and regular and reacted to light. There was slight but definite rigidity of the neck. The heart did not appear to be enlarged. The sounds were of poor quality, but regular; there were no murmurs. The lungs were clear throughout. The abdomen was soft; no masses were felt. The reflexes were normal throughout. The blood pressure was 84 systolic, 56 diastolic.

The temperature was 105.6°F., the pulse 140, and the respirations 40.

Examination of the blood showed a red-cell count of 5,400,000 with a hemoglobin of 85 per cent, and a white-cell count of 18,000 with 84 per cent polymorphonuclears. Eighteen hours after admission, the white-cell count had risen to 30,000. A catheter specimen of urine showed a specific gravity of 1.028, a + test for albumin and some white blood cells and many finely and coarsely granular casts. A blood culture was negative. The nonprotein nitrogen of the blood was 55 mg., and the blood urea nitrogen 29 mg. per 100 cc. A lumbar puncture showed normal dynamics, and the spinal fluid was normal. A Widal test was negative, and cultures of the stools were negative for typhoid and dysentery organisms. An x-ray film of the chest, taken with a portable machine, was negative.

On admission, the patient was given 5 per cent glucose and physiologic saline solution by clysis,

and subsequently, intravenous, rectal and subcutaneous fluids to maintain a daily intake of from 2000 to 3000 cc. Sulfathiazole, 15 gr. every four hours, was continued for the first eighteen hours of the hospital stay but was then omitted. The patient gradually became more responsive, and about twenty-eight hours after admission the temperature had dropped to 101°F. and gradually from there to normal. The pulse dropped only to 110, and the respirations to 25. During the first twenty-eight hours, the urine output by catheter was only 120 cc., but it was believed that the patient voided unmeasured amounts with coughing and with bowel movements.

On the third day, the patient was talkative but very weak. The blood pressure was 86 systolic, 48 diastolic. The cough had become less frequent, but the diarrhea continued. During the next two days, her blood pressure continued to be low but her cough and diarrhea almost disappeared. On the sixth day, the abdomen was slightly distended and tender in the right hypochondrium. Catheterization yielded 400 cc. of dark turbid urine containing many white blood cells and casts. The next day, the temperature was normal and the pulse 104, but the patient became very lethargic. There was persistent tenderness in the right hypochondrium, and bilateral ankle clonus was found. On the eighth day, she could be roused very slightly; catheterization yielded only 100 cc. of urine in eighteen hours, after an intake of 3000 cc. The patient was given an ampule of 50 per cent glucose solution intravenously. The nonprotein nitrogen of the blood rose to 80 mg. per 100 cc., and the following day, immediately after catheterization,—only 100 cc. of urine had been obtained in the previous fifteen hours,—she had sudden respiratory failure and expired.

#### DIFFERENTIAL DIAGNOSIS

DR. EARLE M. CHAPMAN: Why should an apparently healthy woman of fifty-three years have a minor illness in Florida and then come home to die in anuria about ten days after the return of symptoms?

The illness in Florida was called "grippe," but a sudden fever of 102°F. at least suggests that she might have had malaria. However, there are several points that I should like to rearrange to fit a clinical pattern consistent with an acute infection in the urinary tract. First is the fact that she had pyelitis ten years before admission—a disease known to recur when people suffer fatigue and dehydration. Certainly, the environment in Florida and during the drive back home was conducive to both factors. Likewise, the ir-

regular fever, the high white-cell count and the vague symptoms are compatible with pyelitis or even pyelonephritis. Unfortunately, there is no report of the urine at this period of her illness.

Evidently, the single finding of a Type 8 pneumococcus in the sputum led her physician to suspect a pulmonary infection. Although Type 8 ranks about the fifth or sixth most frequent type found in persons with pneumonia, it could well be a harmless inhabitant of the nasopharynx in a person returning from Florida to a New England winter.

With a suspected pulmonary infection and with stiffness of the neck and a semicomatose condition, one thinks of a brain abscess secondary to a diseased lung. Again, we cannot substantiate any such diagnosis by physical examination, chest x-ray film or lumbar puncture; and, of course, we know that sulfathiazole is poorly concentrated in the cerebrospinal fluid and is therefore contraindicated in cases of meningitis or brain abscess.

After receiving 4 gm. (60 gr.) of sulfathiazole, the patient was much worse and was admitted to the hospital in rather poor condition. She was comatose, coughing and behaving in a peculiar manner. There is no description of the scleras or conjunctivas. It is significant that she already had nitrogen retention and a urine containing albumin, white blood cells and granular casts. Adequate fluids were given, but still she did not excrete a proper quantity of urine. Something was evidently wrong—the sulfathiazole was stopped after a total of 8 gm. had been given in a period of about forty-eight hours. Then she seemed to improve, and the temperature returned to normal. However, the pulse continued to be rapid, and the blood pressure became even lower in its maintained or diastolic level. Then there was a cessation of the diarrhea—which explains the need of the previous laboratory studies that were negative.

The signs of kidney failure increased—the urine became turbid and dark and contained many white blood cells. Congestive failure, or some toxic effect, caused distention and tenderness of the liver. Lethargy, drowsiness and coma supervened, and the nonprotein nitrogen reached 80 mg. per 100 cc.; yet the blood pressure remained low. Concentrated glucose did not bring about a diuresis. She died of sudden respiratory failure. I doubt that she had a silent occlusion of a coronary artery as a cause of this.

It is my belief that the patient died in anuria because her kidneys, previously diseased and possibly showing pyelonephritis, did not excrete sulfathiazole properly. It would be helpful to know

the blood level of the drug for the several days after it was stopped. Sulfathiazole is definitely more toxic to the kidneys than the other sulfonamide drugs are. It seems that the kidney tissue was particularly sensitive in this woman, since we have no description of the commonest signs of toxicity—an erythematous skin lesion or reddened conjunctivas. The fever, leukocytosis, diarrhea and mental changes could be part of the reaction. I am not surprised by the absence of anemia. The stiffness of the neck does concern me, and unless we call it meningismus, I cannot explain it.

From reported cases of anuria caused by sulapyridine and sulfathiazole, we know that the chief difficulty is with a plugging of the collecting tubules, or even the ureters at any level, by the drug crystals and secondary detritus. Consequently, microscopic sections have shown great distention and plugging of the tubules, while the glomeruli remained comparatively normal. If such a plugging had occurred in this case, we could expect that cystoscopy and ureteral lavage would have been therapeutically effective.

DR. FLETCHER COLBY: That seems to be a good possibility. On the other hand, is it not quite possible that she just had chronic nephritis of such severe degree that a superimposed acute infection was enough to produce anuria without implicating sulfathiazole?

DR. ALFRED KRANES: The specific gravity of 1.028 is somewhat against chronic nephritis.

#### CLINICAL DIAGNOSIS

Bronchopneumonia?

#### DR. CHAPMAN'S DIAGNOSES

Chronic pyelonephritis.

Sulfathiazole toxicity, with plugging of ureters and tubules of the kidneys, leading to anuria.

#### ANATOMICAL DIAGNOSES

Acute pyelonephritis, bilateral.

Pericarditis, acute.

Myocarditis, acute.

Pulmonary edema and congestion.

Ascites, slight.

#### PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: This patient was studied at another hospital, but the autopsy was performed by one of our laboratory staff. Clinically, because of the finding of the Type 8 pneumococcus in the sputum, a great deal of attention was paid to her chest, and it was believed that she

probably had bronchopneumonia. The autopsy, however, showed no evidence of pneumonia, just a little edema and congestion of the lungs. Her kidneys were large, weighing 385 gm. The capsules stripped fairly easily, and the surfaces showed a reddish mottling and few grayish-white spots that suggested small abscesses. The sections microscopically showed a diffuse acute pyelonephritis. The tubules were filled with red and white cells, and there were a number of small abscesses throughout the kidney. We specifically looked for sulfathiazole crystals and could not find any, either grossly or microscopically. The severe degree of pyelonephritis, however, was enough to have produced the renal insufficiency. We have

had this year, I believe, four cases of acute pyelonephritis, very similar to this, in which the signs and symptoms did not particularly point to the kidney. The only clue here was the presence of leukocytes in the catheterized specimen. Unfortunately, the urine was not cultured. There was about 50 cc. of turbid fluid and a few shreds of fibrin in the pericardial cavity, and sections of the myocardium showed a few collections of polymorphonuclears. Bacteriologically, we were able to grow nonhemolytic streptococci from the kidney and spleen.

DR. JOHN H. TALBOTT: Did the patient have a cerebral abscess?

DR. CASTLEMAN: The brain was not examined.



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## MATERNAL WELFARE AND THE NATIONAL EMERGENCY

World War II is inevitably forcing the country to face a national emergency in maternity care. Already the armed forces have taken large numbers of physicians into service, and future estimates call for nearly half of today's active practitioners. This need must be met. But equally so, maternal care must not be jeopardized. The totalitarian countries have been quick to realize this, for their armies of the future can exist only in the babies of today. To them, the mother and her child are irreplaceable assets. One must hope that in lands granted the opportunity of building for a peaceful, productive future, maternal welfare will be no less zealously guarded.

The problem in this country is not a new one. Ever since the introduction of routine prenatal examinations in the early years of this century, more and more attention has been paid to organized maternal care. The result has been a gratifying but by no means satisfactory reduction in maternal deaths and morbidity. Even in 1939, there were over 12,000 live births without medical attention. Less fortunate still were those women cared for by practitioners of meddling obstetrics. It is clear that further decrease in mortality and morbidity rates will come only through an improvement in the quality of obstetric care and in its extension to the entire population. Ideally this should be provided by a sufficiently large number of physicians well trained in obstetrics. An all-out program of this sort would include a more thorough undergraduate obstetric training, adequate postgraduate educational opportunities, adjunct obstetric nursing services, improved hospital facilities, lay education, consultation services, and an organization of medical facilities to bring all economic and geographic units within the scope of the program. Thus, every pregnant woman would be cared for by a physician basically well-trained in obstetrics, with all possible specialized assistance at hand whenever needed. This goal has never been reached; when it may be attained in the future one cannot foretell. With the removal of ever-increasing numbers of physicians from civilian life the date will be further postponed. But the problem is one of the immediate present. In solving it, America might do well to turn to the midwife. Her help now and in the reconstruction to follow would be invaluable; it is probable that in certain capacities she would become part of the permanent obstetric service of the nation.

Although the midwife never has been much favored in the United States, she still delivers more than half the babies of Europe. She has played her part in the notably low mortalities of the Netherlands and Scandinavia. Midwifery services in the United States as well have demonstrated that they can offer safe pregnancy care. The Frontier Nursing Service of Kentucky covers

seven hundred square miles of territory in mountainous Leslie County and has delivered over 3000 babies, with a gross uncorrected maternal mortality of 0.68 per 1000 live births—the mortality rate for the country as a whole approximately 4 per 1000. The Philadelphia Wives Service shows a mortality rate of half of the city as a whole. Louisiana has reduced its maternal mortality significantly through obstetric care offered by its colored midwives. The Outpatient Department of the Boston Lying-in Hospital, manned by externs, has a rate of 0.15 per 1000 home deliveries: this and similar departments elsewhere are basically midwifery services. It must be noted, however, that these results have been obtained only with carefully and rigidly controlled systems under competent medical supervision, with proper hospital facilities in the background. Furthermore, it is clear that the best figures come from the services staffed by the modern type of midwife.

The new order of midwife is a graduate nurse who has had additional formal training in obstetrics. In training, therefore, she stands between the obstetric nurse and the obstetrician. She may hold the certificate of the Central Midwives Board of Great Britain or be a graduate of the Lobenstein School, of New York City, or of the newly founded school of the Frontier Nursing Service; she will undoubtedly find other schools offering similar courses. She is licensed as carefully as the physician. Over her and working with her are competent consulting obstetricians, and always there is access to a hospital. Cases are registered early with her service and are selected according to anticipated difficulties. Patients with complications are hospitalized before they become serious problems. Emergencies are

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ects to which the institute can address itself. The city dweller is well protected against polluted water, infected food and incompetent systems for sewage disposal, but he is allowed less sunlight, is forced to inhale more foreign materials, is exposed to a greater variety of respiratory viruses and probably subjects himself to a greater and more frequent climatic variation than does the man on the farm. The health authorities of all our large cities are also now concerned with housing, with transportation facilities, with transient populations and with an ever widening field of application for the knowledge and understanding of environment.

Starting out with a relatively modest budget, the institute will have a splendid opportunity to prove itself. Provisions have been made for it to receive and accept grants, gifts, bequests and contributions from private citizens and foundations. Its future scope is thus not limited or altogether dependent on the expediences or political necessities that have been known to cramp many other governmental enterprises. If the largest city in the world finds that a public health research institute is of value, other cities will surely follow suit, for the largest city has no monopoly on municipal problems concerned with the health and welfare of the citizens. It is hoped that this new type of research motive will prove successful.

## MEDICAL EPONYM

### JOFFROY'S SIGN

'Nature et traitement du goitre exophtalmique [The Nature and Treatment of Exophthalmic Goiter]' was the subject of a lecture delivered by Alexis Joffroy (1844-1909) in December, 1891, in the neurological clinic of the Hospice de la Salpêtrière. This lecture appears in *Progres médical* (18: 477-480, 1893). A portion of the translation follows:

*Paralysis of the muscles of the upper part of the face.* In our patient, these muscles were affected in a peculiar way that I have seen previously in three other cases although this peculiarity has never been pointed out before. It is as follows: if a person who is looking downward is asked to look up at the ceiling quickly, holding his head still, it will be found that as the eye balls roll upward, the eyebrows are raised and the forehead wrinkles. We have here a synergic movement occurring in the normal state that does not occur in this patient. Her eyebrows and forehead remain abso-

lutely immobile, even when she tries very hard to look upward.

R W B

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

#### FATAL SEPSIS FOLLOWING ABORTION

A twenty seven year-old para V, approximately three months pregnant, was admitted to the hospital with a high temperature and with a catheter protruding from the vagina.

The past history contained no pertinent details. The patient had apparently had no prenatal care. Physical examination was essentially negative except for the elevated temperature, a corresponding rise in pulse rate, and tenderness and spasm over the entire lower abdomen. The patient was having cramplike pains, and a few hours later delivered herself spontaneously of a macerated fetus and the placenta. Following delivery, she had a chill, which lasted ten minutes. The temperature ran a high septic course, and the patient developed jaundice. The treatment consisted in several transfusions, the uterus being left entirely alone. Death occurred on the eleventh day after admission.

Autopsy revealed extensive jaundice, the uterus was necrotic from the cervix to the fundus, the spleen was enlarged to twice its normal size, the left ovary and tube were necrotic, and the right ovary and tube were infected.

*Comment.* There is nothing in this history to reveal whether this was a criminal abortion or one brought on by the introduction of a catheter by the patient herself. When she arrived at the hospital, she was septic, and she died of profound sepsis ten days later. The jaundice was characteristic of that sometimes associated with infection, and the infection of the uterus, tubes and ovaries was typical of the sepsis that often follows abortion. This death occurred before the introduction of the sulfonamide drugs, and it is possible that intensive chemotherapy might have averted this death.

As in many of these cases, this patient was probably treated by an abortionist. The end result is one that may follow any criminal abortion—a tragedy that, if generally recognized, might prevent some women from looking on this procedure with perfect nonchalance.

\*A series of selected case histories by members of the section will be published weekly. Comments and queries by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, Secretary, 350 Dartmouth Street, Boston.

DEATHS

ALBEE — GEORGE M. ALBEE, M.D., of Worcester, died August 10. He was in his seventy-first year.

He received his degree from the New York University Medical College in 1893, and had practiced in Worcester for many years, having been particularly interested in cardiology.

Dr. Albee was a fellow of the Massachusetts Medical Society and the American Medical Association. He was also a fellow of the American College of Physicians, and a member of the New England Heart Association and the American Heart Association.

LORD — WILLIAM O. LORD, M.D., of New Bedford, died August 8. He was in his sixty-first year.

Born in New Bedford, he received his degree from the Columbia University College of Physicians and Surgeons in 1903.

He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a son, a half-brother and two half-sisters survive him.

REPORT OF MEETING

NEW ENGLAND PATHOLOGICAL SOCIETY

A regular meeting of the New England Pathological Society was held on April 17, Dr. Traey B. Mallory presiding. Dr. Arthur Purdy Stout, associate professor of surgery at Columbia University and attending surgical pathologist to the Presbyterian Hospital in New York City, spoke on "Tumors of Peripheral Nerves." Dr. Stout divided the tumors of the peripheral nerves into six groups (Table 1), and the discussion dealt chiefly with

this mesectoderm forms adult connective tissue and cartilage.

These observations form a solid foundation for the hypothesis that most of the primary nerve-sheath tumors are of neurectodermal origin and composition. They explain the connective-tissue fibers of the neurilemmoma, neurofibroma and malignant neurilemmoma (schwannoma) and the bone and cartilage of the teratoid tumors of peripheral nerves. Further confirmation comes from the fact that Dr. Murray has grown almost pure cultures of schwannian cells from neurilemmomas and neurofibromas and from one case of malignant neurilemmoma (schwannoma). The formation of adult ganglion cells by ganglioneuromas and of true rosettes by neuroepitheliomas establishes their neurectodermal origin. The neurectodermal origin of the pigmented skin tumors is suggested by the observations of Masson and Laidlaw, but the speaker did not accept it as proved.

According to Dr. Stout, primary neoplasms of purely mesodermal origin include hemangiomas and lipomas. Whether ganglions, neuroxanthomas, fibromas and so-called "neurogenic sarcomas" are true nerve-sheath tumors of mesodermal origin is open to debate. He denied that there is adequate proof that ganglions (similar to the familiar ganglions of the wrist), fibromas and xanthomas ever grow in or from peripheral nerves. Proof is also lacking that any of the malignant spindle-cell tumors that form connective-tissue fibers and grow in or from the peripheral nerves are of mesodermal origin. Therefore, until such proof is forthcoming, the use of the term "neurogenic sarcoma" is not justified.

The discussion was opened by Dr. Orville T. Bailey, who confessed his bewilderment concerning the histogenesis of the nerve-sheath tumor. He believes that new methods of study must be developed before any decision can be made; he stated that the work of Dr. Stout and

TABLE 1. Tumors of Peripheral Nerves.

NON NEOPLASTIC NEURECTODERMAL TUMORS	MESODERMAL NEOPLASMS
Traumatic or amputation neuroma	Hemangioma
Spontaneous neuroma	Lipoma
Appendiceal neuroma	(Ganglion?)
	(Neuroxanthoma?)
	(Fibroma?)
	("Neurogenic [neurogenous] sarcoma"?)
NEURECTODERMAL NEOPLASMS	TUMORS AND LESIONS WHOSE GROWTH IS INDUCED BY
Neurilemmoma	NEUROGENOUS TUMORS
Neurofibroma	Fibroma molluscum
Ganglioneuroma	Multiple adenoma sebaceum
Neuroepithelioma	Elephantiac hypertrophy of bone, intestine,
Malignant neurilemmoma	appendix and so forth
Teratoid tumor	Hypertrichosis
(Pigmented mole and melanoma)	Skin pigmentation
(Mesectodermoma?)	Multiple lipomas
NEOPLASMS COMPOSED OF MULTIPLE TISSUES OF WHICH	SECONDARY NEOPLASMS
NEURAXONS FORM ONE IMPORTANT ELEMENT	Direct extension within nerve sheath
Glomus tumor	Intra-neural metastasis
Cutaneous leiomyoma	Tumors of ganglia lying within nerves

the question of the cellular origin and the composition of the primary neoplasms. The work of Masson and Nageotte and the tissue-culture observations of Dr. Margaret Murray suggest very strongly that the dominant tissue of the nerve sheath is the neurectodermal schwannian syncytium. This grows in a characteristic fashion in vivo and in vitro, and can form reticulin fibers. The fact that the schwannian cells of the nerve sheath can form connective-tissue fibers need cause no surprise, since it is well known that the cells of the neural crest form connective tissue (mesectoderm) in the human embryo. In urodeles,

Dr. Murray had opened up new possibilities that may do a good deal toward clarifying the situation. He pointed out that there is one problem, without the solution of which one cannot consider the problem of histogenesis completely solved — namely, the occasional resemblance of nerve-sheath tumors to meningiomas. Of course, both types of tumor vary a good deal in histologic structure, and if one acquires a large series of both tumors and arranges them in a graded series, the two extremes are very different; there is an overlapping stage, however, indicating that somehow or other the problem

of the histogenesis of the two is related. Also, the appearance of multiple meningiomas in patients with multiple neurofibromatosis is another indication of their possible relation. If one has only a small fragment of tissue to examine, it is possible to find areas that are almost entirely composed of schwannian cells in the gangliogliomas occurring outside the central nervous system. The occurrence of these areas was very striking in a case reported by Cushing and Wollbach some time ago, in which the diagnosis for a long time was obscured by this difficulty. Dr Bailey believes that the description of the neuroxanthoma suggests strongly that one of the forms of sclerosing hemangiomas is involved. Some hemangiomas are associated or occur in the immediate vicinity of pigmented nevi, and the formation of giant cells and lipid phagocytes is a part of the sclerosing process that goes on in many hemangiomas. Furthermore, this explains very well the histologic appearance of infiltration. The hemangioma has not infiltrated surrounding tissue, but adjacent connective tissue has been stimulated to form its stroma. The glomus tumors, according to Dr Bailey, include a large number of nerve fibers that are the integral part of the tumors themselves. In addition, they have glomus cells that appear to be derived from the smooth muscle elements of the normal glomus. The combination of these fibers and cells not only results in a complex tumor from the morphologic point of view but actually takes on the function of a gigantic glomus.

Dr Stout commented on Dr Bailey's discussion and said that Dr Murray had also been attempting a study of meningiomas from a tissue culture point of view. There are different kinds of meningiomas, and they show quite different characteristics. Cultures of what seem to be meningeal schwannian-cell tumors resemble cultures of schwannian peripheral nerve tumors, they are otherwise quite different. Dr Murray has also had an opportunity to grow three glomus tumors, and they have been extremely interesting in tissue culture because they have grown out endothelium that could be recognized quite easily *in vitro*. They have also grown out schwannian cells, which is to be expected because there are so many nerves in the glomus tumors. Finally, they have grown out the so-called "epithelioid cells." These have done a very interesting thing in culture. When endothelium has grown out in long thick syncytial masses, the epithelioid cells of the glomus tumor attach themselves in clusters to the endothelium. Therefore, the relation of the epithelioid cells to the smooth muscle cells that Dr Bailey spoke about is very possible. Drs Stout and Murray were fortunate enough to get hold of an infiltrating glomus tumor and grow it *in vitro*, and it behaved in exactly the same way as the benign glomus tumors. Dr Stout had never before come in contact with an infiltrating glomus tumor, but apparently it was genuine.

Dr Robert Gross continued the discussion by stating that in the classification of the neuroectodermal tumors Dr Stout mentioned neurilemmoma and malignant neurilemmoma. Dr Gross believes that the malignant neurilemmomas might be further divided, because in reviewing the specimens at the Peter Bent Brigham and Children's hospitals, it was evident that some have more malignant qualities than others, so far as the clinical characteristics are concerned. He said that the benign tumors are called "neurilemmomas," the middle group malignant neurilemmomas, and the more malignant ones "neurogenic sarcomas," although he acknowledged that these terms are in correct, in comparison with their use by other pathologists. In the middle group, the findings are not the

same as those in the rank and file of sarcomas. This type of neoplasm tends to recur locally but does not metastasize. It can be recognized histologically in that the cells have more cytoplasm than those of the neurilemmoma, the fibers are shorter, the nuclei are vesicular, and they may have occasional mitotic figures. Dr Gross stated that he had seen four of these tumors. One, of the fifth nerve, was in a thirty-two-year-old woman who had recurrences in spite of five or six attempts at removal and heavy x-ray therapy. Another, in a thirty-year-old woman with a tumor of the left subscapular nerve, which was locally excised, recurred, and two years later a further excision was done. This went on for fourteen years before massive local recurrence extended into the thorax. The third patient was a child with a lesion of the little finger. The tumor recurred after six local operations, and finally ended with removal of the ulnar half of the hand. The last case encountered was that of a twenty-three-year-old man with an egg-sized tumor of the posterior cord of the brachial plexus. Since, histologically, this tumor had the same characteristics that were used for placing neoplasms in this group of malignant neurilemmoma, local excision by peeling it out from the cord was not done, but the entire posterior cord was removed. There has been no evidence of recurrence. Dr Gross considers it essential to recognize this group because of the practical considerations involved. In other words, these tumors do not need to be treated by amputation, as neurogenic sarcomas that occur in extremities do, and conversely cannot be treated properly by enucleation, as one does in a benign tumor (neurilemmoma), by peeling it out from the sheath. Therapy must lie between the more radical and conservative forms, in other words, the entire mass, with nerve trunk, must be excised.

Dr Stout admitted that the classification of malignant neurogenous tumors used is not sufficiently complete. He thinks that it is probably necessary to subdivide the malignant neurilemmomas, or schwannomas. He added that most of these, as Dr Gross had said, are malignant by infiltrative growth, and very few of them metastasize. Dr Stout is as yet unable to subdivide them into grades of malignancy.

Dr Donald Murnaghan, of Ireland, stated that a few days previously Dr Murray had very kindly shown him some of her preparations, some were living, others fixed and stained. His own experience, from studies made in the laboratory of Dr Warren Lewis in the Carnegie Institute of Washington at Baltimore, was in complete agreement with her identification of schwannian cells. He recognized the same type of cell in chick embryo and mouse embryo material and noted the similarity between them, the satellite cells of spinal ganglion cells were tentatively identified as oligodendroglial, the latter in cultures of the central nervous system. In cultures of embryonic peripheral nerves, rapid outgrowth of mesenchymal cells soon obscured the migrating schwannian cells, and he did not follow them. His experience did not extend to adult issues, and therefore he did not express an opinion on Dr Murray's work in this field, except to acknowledge her ability to distinguish schwannian cells from fibroblasts. Embryologists believe that oligodendroglia and schwannian cells arise from equivalent sources in the neural ectoderm, a term that should be used with reservations because it is now believed that the time-honored, three-germ layer is more a convenient than an accurate representation of the true state of affairs in the young developing embryo. Histologists are familiar with the similarity between spinal ganglion satellite cells and the sheath cells

of Schwann, and now cytologists find certain morphologic and cultural characteristics common to all three. He stated that oligodendroglia, the satellite cells of spinal-ganglion cells and schwannian cells, are morphologically equivalent, showing similar characteristics, embryologic, structural and cytologic. He then showed in a motion-picture film how oligodendroglia grow out in a culture of the midbrain of a seven-day chick embryo, in a fluid medium, and to indicate the method of locomotion so beautifully demonstrated by some of these cells.

Dr. Tracy B. Mallory continued the discussion. He said that a pathologist is often called on by the surgeon to give an opinion regarding therapy in local recurrence, since it is known that some tumors metastasize. Often, a patient comes in who has had one or two or even three recurrences of definite malignant types. The question comes up whether amputation or another local excision should be done. He asked Dr. Stout to say a little more about treatment, about radiation of the malignant type and also how the acoustic neuromas fitted into his classification.

Dr. Stout answered that if the tumor is a malignant form occurring in von Recklinghausen's disease, practically none have been cured either by excision or amputation. Possibly the reason for that is that von Recklinghausen's disease is a generalized disease in which many nerves are involved, and if one succeeds in removing one of them that seems to be malignant at the moment, the tendency to form malignant tumors in that patient is great enough for other tumors to form further progressive growths. When they occur without von Recklinghausen's disease, the indication is to try to get rid of the local growth. If its extent is so wide as to necessitate amputation, one should not hesitate to advise amputation. From personal experience and reading, Dr. Stout believes that none of these tumors are radiosensitive, and that none are destroyed by irradiation. The very rare neuro-epitheliomas are extremely malignant metastasizing tumors, and the most radical form of treatment is indicated.

Dr. Stout remarked that he had seen fewer acoustic tumors than tumors farther away from the central nervous system. Those that he had seen appeared to be neurilemmomas. They show some variance and have a much greater tendency to have cells containing lipoid than the peripheral tumors, in which lipoid is only occasionally found. He said that Dr. Murray has grown three angle tumors *in vitro*, and that they, too, grew out cells that were interpreted as schwannian cells.

## BOOK REVIEWS

*Radiologic Physics.* By Charles Weyl, M.S.; S. Reid Warren, Jr., Sc.D.; and Dallett B. O'Neill. With a foreword by Eugene P. Pendergrass, M.D. 8°, cloth, 460 pp., with 166 illustrations and 33 tables. Springfield, Illinois: Charles C Thomas, 1941. \$5.50.

This book deals with those branches of physics that are met with in the study and application of radiant energy. It also covers, but to a lesser extent, the other types of electrical apparatus found in the modern hospital. As noted in the introduction, the book attempts to bridge the gap between no knowledge of physics and advanced specialization. To the reviewer, such a bridge is too long for a single span. The major portion of the book contains material that is too far advanced for the average practitioner or student of radiology, who has no special bent for the physical problems related to his

specialty, and it is apparently designed for the person who is doing research work in this subject. The first two chapters of the book, on the other hand, deal with material encountered in the most elementary courses of science in high schools, and there is an appendix of forty pages containing the elements of algebra, trigonometry and calculus.

There is a good discussion of the methods of measurement of quantity and quality of radiant energy, but too brief a discussion of the use of metal filters. Only a part of one chapter has been devoted to discussion of the circuits commonly used in x-ray generators, and there are only a few remarks concerning the advantages and disadvantages of the various types.

On the whole, the book seems not to provide a satisfactory source of information for the average student radiology who wishes to know something of the machines with which he works.

*Blood Transfusion Association Report: Concerning a project for supplying blood plasma to England, which has been carried on jointly with the American Red Cross from August, 1940, to January, 1941.* 8°, paper, 121 pp. New York: Blood Transfusion Association, 1941.

A blood-transfusion association has been operated in New York City since 1929, with the principal object improving the supply of blood for transfusion purposes in that city. In June, 1940, in conjunction with the American Red Cross, the association greatly expanded its work to supply blood plasma for England. In a period of six months, its members collected over 5000 liters from about 15,000 persons, and much of this plasma was sent to England. After the first of January, 1941, England was able to supply its own needs, and the organization closed down this part of its work. Wisely, however, research concerning the advantages and disadvantages of blood plasma or blood serum, both in the liquid and the dried states, has been continued, and this work is to be carried on until more definite conclusions can be reached. The report of this six-month endeavor contains much valuable information about the organization of the work, and is a medical report of great value. It is a welcome addition to the literature.

*Applied Physiology.* Oxford Medical Publications. Samson Wright, M.D., F.R.C.P. Seventh edition. 10 cloth, 787 pp., with 367 illustrations and 5 color plates. New York: Oxford University Press, 1940. \$7.00.

Since the first edition of this commendable textbook published in 1926, the author has been consistent in his aim to present the facts of physiology for use by men working in the wards and various other departments of hospitals. This new edition has been drastically revised by the incorporation of recent advances in this science. As a member of the editorial staff of Section A-III of the *British Chemical and Physiological Abstracts*, the author was particularly well placed for the task.

The book has been enlarged, and contains five color plates and many illustrations. Students will find many cross references of recent investigations, inserted throughout the text. It may be noted that the author has not lost sight of the academic aspect of physiology in his emphasis on its applied aspects.

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## PERICARDIOSTOMY FOR SUPPURATIVE PERICARDITIS\*

A Report Concerning Ten New Cases and Twenty-Eight Cases from the Literature

JOHN W. STRIEDER, M.D.,<sup>†</sup> AND WILLIAM R. SANDUSKY, M.D.<sup>‡</sup>

BOSTON

DURING the last half century, there have been numerous contributions to the literature dealing with suppurative pericarditis. In recent years comprehensive reviews by Shipley and Winslow,<sup>1</sup> Bisgard,<sup>2</sup> Truesdale<sup>3</sup> and others have summarized the present knowledge of the subject and have collected the recorded cases treated by pericardiostomy. Thus, up to January 1, 1934, Shipley and Winslow<sup>1</sup> were able to collect 227 cases. In this series, there were 102 deaths, a mortality of 44 per cent.

In this paper, we report 5 cases of acute suppurative pericarditis in which pericardiostomy was performed by one of us (J.W.S.), record 5 additional cases from the records of the Boston City Hospital, and review a series of 28 cases collected from the literature from January 1, 1934, to January 1, 1940. The addition of these cases from the Boston City Hospital brings the total of the recorded cases to 265. The 10 reported cases are summarized in Table I, and the 28 collected cases in Table 2.

The frequency of the disease is emphasized by Pyrah and Pain,<sup>27</sup> who found acute pericarditis in 214, or 2.7 per cent, of 7965 autopsies performed at the Leeds General Infirmary from 1921 to 1931. Of these, 91, or 1.1 per cent of all cases, were classified as acute suppurative. This figure is supported by an incidence of 177 cases, or 1.8 per cent, described as acute suppurative among 9536 autopsies performed at the Boston City Hospital from 1916 through 1938. In the same trend is a figure of 1.1 per cent of 1795 autopsies at the Massachusetts Memorial Hospitals. Stenbuck<sup>12</sup>

states that in the nine years prior to December, 1936, there were 4000 autopsies at the Mt. Sinai Hospital. In this series, there were 67 cases of acute purulent pericarditis, in which only 1 patient had been operated on. Many of the cases in this series were, of course, a single manifestation of an overwhelming sepsis and, as such, were but an incident in the progress of the fatal illness.

Notwithstanding the frequency of its occurrence, Cabot<sup>28</sup> states that 77 per cent of all cases of pericarditis, found at autopsy at the Massachusetts General Hospital were not diagnosed during the life of the patient. These figures, however, are somewhat misleading because, although these cases are termed acute pericarditis, they were not all purulent. Thus, it seems to us that cases amenable to surgery might have a higher percentage of correct diagnoses, since, as mentioned above, many cases termed acute pericarditis are incidental and, indeed, terminal.

This impression is confirmed by Bigger<sup>22</sup> in analyzing 17 cases of acute fibrinopurulent or purulent pericarditis from the Medical College of Virginia Hospitals. Seven of the frankly purulent ones were correctly diagnosed, and 6 were drained. Of the remaining 10, first diagnosed at autopsy, only 4 had a demonstrable increase in pericardial fluid, and in the other 6, death occurred from an overwhelming infection before there had been an opportunity for pus to form in the pericardial sac. All 4 of the patients who were found on post-mortem examination to have a demonstrable increase in fluid were moribund when admitted to the hospital, 3 dying in less than twelve hours and 1 in twenty-four hours.

Since the disease is never primary, except in the sense that it occurs as a complication of direct trauma (although Morin<sup>4</sup> has reported a case that

\*From the Surgical Services of the Boston City Hospital. Read in part before the annual meeting of the Massachusetts Medical Society, May 21, 1940.

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<sup>‡</sup>Formerly, resident surgeon, Second Surgical Service, Boston City Hospital.

TABLE 1. Data on Reported Cases.

CASE NO.	DATE	AGE	SEX	ORGANISMS	DURATION OF ILLNESS	ANTECEDENT DISEASE	PHYSICAL SIGNS	X-RAY	TAP	TYPE OF OPERATION	DRAINAGE MATERIAL	IRRIGATION	RESULT
1	1937	48 yr.	M	Type 8 pneumococcus	4 days	Pneumonia (left lung)	Diagnostic (rub)	Diagnostic	+	Resection left 4th and 5th cartilages	None	Saline solution	Died, 10 days (septicemia)
2	1938	13	F	<i>Staph. aureus</i> (hemolytic)	12 hours	Pneumonia, septicemia	Diagnostic (rub)	Not diagnostic	+	Resection left 4th and 5th cartilages	None	Saline solution	Died, 42 hours (septicemia)
3	1939	33	M	<i>Staph. aureus</i>	4 days	Stab wound	Diagnostic (no rub)	Diagnostic	Not done	Resection left 5th and 6th cartilages	None	Dakin's solution	Recovered
4	1940	44	F	<i>Staph. albus</i>	2 days	Ulcerative colitis	Diagnostic (rub)	Not diagnostic	+	Resection left 5th and 6th cartilages	None	Dakin's solution	Died, 7 days (septicemia)
5	1940	15	M	Type 5 pneumococcus	Few hours	Lobar pneumonia (left lung)	Diagnostic (rub)	Diagnostic	No fluid obtained	Resection left 5th and 6th cartilages	None	Dakin's solution	Recovered
6	1913	30	M	Pneumococcus	Few hours	Pneumonia (right lung)	Diagnostic (rub)	Diagnostic	+	Resection right 4th and 5th cartilages	Cigarette	None	Recovered
7	1917	17	M	?	28 days	Bilateral empyema	Diagnostic (no rub)	Diagnostic	+	Resection left 5th cartilage	Rubber tissue	None	Died, 28 days (pneumonia)
8	1921	14	F	<i>Staph. aureus</i>	1 day	Septicemia	Diagnostic (no rub)	Diagnostic	+	Resection left 5th and 6th cartilages	Rubber tube and gauze	None	Died, 23 days (pulmonary edema)
9	1929	18	M	<i>Staph. aureus</i>	2 days	Broncho-pneumonia	Diagnostic (no rub)	Diagnostic	+	Resection left 6th and 7th cartilages	Rubber tube	Saline solution	Recovered
10	1930	12	M	Type 1 pneumococcus	Few hours	Lobar pneumonia and empyema (right lung)	Diagnostic (no rub)	Not diagnostic	+	Resection of one cartilage (closed drainage)	Rubber tube	Dakin's amniotic fluid	Died, 15 days



he considers primary), pericarditis may well be obscured by the original infection, particularly, as is so often true, if this infection is within the thorax. Thus, in our 10 cases, 7 were secondary to pneumonia or empyema, or both; 2 were secondary to septicemia, and 1 followed a stab wound. Twenty-seven of the 38 cases reported since 1934 followed affections of the chest, as shown in Table 3. Although it is not the purpose of this paper to go exhaustively into diagnosis, one cannot but assume, in the light of the foregoing, that an improvement in diagnosis will be obtained only if the physician, in the absence of localizing symptoms, makes careful repeated examinations of the cardiac region. Further, as Bigger<sup>23</sup> points out, if a friction rub is not heard and there is no appreciable increase in the amount of intrapericardial fluid, the diagnosis cannot be made. No rub was heard in 5 of our 10 cases. The roentgenographic and fluoroscopic findings may, therefore, be of no diagnostic aid in a certain percentage of cases, and this was true in 2 of the 10 cases that we report. Nevertheless, roentgenographic examination is of the utmost importance in diagnosis and should be carried out in the upright and prone positions, as suggested by Hodges,<sup>24</sup> so that alterations in the pericardial shadows resultant on these changes in position may be observed.

Heyl<sup>9</sup> has described fluid waves moving down the borders of the pericardial shadow, initiated by systole, that he observed fluoroscopically and that he considered pathognomonic of fluid in the pericardium. Not infrequently, the patient is too ill to permit careful fluoroscopy.

In cases of questionable diagnosis, one may have recourse to pericardicentesis or exploratory operation. Although the former procedure carries undeniable risks (we have seen unwitting puncture of an enlarged heart result in death from hemo-pericardium with cardiac tamponade), we believe it should be carried out before exploration is undertaken. It was performed without incident in 9 of our 10 cases, and, in the case in which it was not performed (Case 3), pus draining from the stab wound established the diagnosis.

On the basis of our personal experience and the recorded cases, we cannot agree with Elkin,<sup>30</sup> who believes it is safer to expose the pericardium by operation than to perform pericardicentesis. Although we agree that pericardiostomy is, itself, attended by little or no risk, we should qualify this by stating that, if fluid is not obtained by pericardicentesis after one or two attempts, further efforts should be abandoned in favor of exploration, particularly if the patient is suffering from the effects of cardiac tamponade.

It is well known that post-mortem examination of patients dying of pneumonia and its complications may reveal a varying accumulation of sterile fluid in the pericardium while there is, at the same time, actual pus in one or both pleural cavities. This has been particularly likely to occur since the advent of chemotherapy. Finland<sup>21</sup> offers the suggestion that the diffusion of the drug into the pericardial fluid suffices to kill such organisms as traverse the pleura and pericardium, whereas the initial or continuing infection of the pleura cannot be taken care of because of a low concentration of the drug, the great number and virulence of the organisms or an excessive amount of so-called "inhibiting substance" in the infected pleural cavity. All three of these factors may operate simultaneously.

This chain of circumstances, when present in a patient who has clinical evidence of acute pericarditis, may pose a nice question of judgment, and was actually encountered in 2 of our patients (Cases 5 and 9). Thus, if organisms cannot be demonstrated in the pericardial fluid obtained by pericardicentesis, and the patient has an empyema, or has had pneumonia, and is clinically suffering from the effects of pericarditis, should pericardiostomy be undertaken?

Of course, one cannot answer this question categorically. We believe that there are sound reasons for proceeding with operation in the face of this negative evidence, because of the considerable advantages to be derived from drainage before the pus becomes thick and fibrinous. We have found this to be true in 3 cases in which the patients were operated on before thick pus had formed (Cases 4, 5 and 9); all recovered. Certainly, one cannot know whether the fluid will remain sterile or become purulent, but if the patient is relieved by pericardicentesis and the fluid remains clear, one is, perhaps, justified in repeating the aspiration and observing the character of the fluid for a day or two longer.

#### TREATMENT

Although it has been stated that suppurative pericarditis, unoperated, has a mortality of 100 per cent, this is not strictly true, since cases of spontaneous evacuation, with recovery, and of recovery after repeated pericardicenteses can be found in the literature. The percentage of such cases, of course, must be extremely small, and it is to be regretted that, with the advent of the use of sulfanilamide and related compounds, probably increasing numbers of ill-advised trials of such non-operative measures will be made. It is only the occasional patient with empyema thoracis who recovers with aspiration alone or in combination

TABLE 2. *Data on Collected Cases.*

CASE No	AUTHOR	SEX	AGE yr.	PRE EXISTING DISEASE	ORGANISM	OPERATION	RESULT	COMMENT
11	Morin <sup>4</sup>	M	18	None	<i>Staphylococcus</i>	Pericardiectomy	Died, 2½ months after onset of disease	Autopsy revealed no case of infection. Authors believe this is a case of "primary pericarditis."
12	Sennels <sup>5</sup>	M	16	Infected left knee	?	Resection of ensiform	Died, 10 days after operation	Multiple metastatic abscesses
13	Gertzenstein and Kreutzer <sup>6</sup>	M	7	Infected right knee	?	Pericardiectomy	Died, 10 days after operation	Autopsy "bacillary arthritis" (right knee)
14	del Carril, Pflaum and Dechessari <sup>7</sup>	M	1¼	Pneumonia and empyema	<i>Pneumococcus</i>	Resection of 5th left cartilage	Died, 12 days after operation	
15	Moore <sup>8</sup>	M	12	Pneumonia and empyema	Hemolytic streptococcus	Posterior resection, 5th and 6th ribs	Recovered	Pleural cavity obliterated by previous empyema
16	Heyl <sup>9</sup>	F	1½	Pneumonia (right lung)	Type 4 pneumococcus	Resection left 3rd and 4th cartilages	Recovered	Measles previous to pneumonia
17	Plasecki <sup>10</sup>	F	8	Pneumonia and empyema (left)	<i>Pneumococcus</i>	Resection left 5th cartilage	Recovered	
18		M	10	Pneumonia and empyema (left)	<i>Pneumococcus</i>	Resection left 5th cartilage	Recovered	
19	Wilensky and Lilienthal <sup>11</sup>	F	6	Septicemia and empyema (right)	Nonhemolytic streptococcus	Resection right 5th and 6th cartilages	Recovered	Approached on right side because of right empyema
20	Stenbuck <sup>12</sup>	M	5	Bilateral empyema	Type 2 pneumococcus	Resection left 4th and 5th cartilages	Recovered	Drainage of right empyema and of left pyopneumothorax, with bronchopleural fistula and tens on symptoms
21	Bigger <sup>13</sup>	M	14	Bronchogenic carcinoma	<i>Staph aureus</i>	Resection left 5th and 6th cartilages	Died, 21 days after operation	Previous pneumonectomy
22		M	12	Septic arthritis and septicemia	<i>Staph aureus</i>	Resection left 4th and 5th cartilages	Died, 3 days after operation	
23		F	10	Pneumonia and empyema (right)	Nonhemolytic streptococcus	Resection left 4th and 5th cartilages	Recovered	Empyema (right) drained by closed method, 6 days after pericardiectomy
24		M	16	Tuberculous pericarditis with secondary infection	Nonhemolytic streptococcus	Resection left 5th and 6th cartilages	Died 4 months after operation	One month before death had lysis of adhesions about inferior vena cava
25		M	18	Pneumonia and empyema (right)	<i>Pneumococcus</i>	Resection left 4th and 5th cartilages	Recovered	Infection of cartilages which prolonged convalescence
26	Sicard <sup>14</sup>	F	12	Pneumonia (right)	<i>Pneumococcus</i>	Epigastric approach (Allingham)	Recovered	Author impressed by the epigastric approach
27	Halloek <sup>15</sup>	M	21	Pneumonia (left)	Type 1 pneumococcus	Through 4th left intercostal space	Recovered	
28	Lilienthal <sup>16</sup>	M	54	Calcified pericardium	<i>Staph albus</i>	Sternum split as for pericardiectomy	Died, 2 weeks after operation	
29	Heidenreich, del Sel and Echevarria <sup>17</sup>	M	30	Pneumonia and empyema	<i>Pneumococcus</i>	Type not stated	Died, 3 days after operation	
30	Ortiz Lagunes <sup>18</sup>	M	35	? Pneumonia	"Of the nature of colon bacillus"	Resection left 6th cartilage	Still in hospital and draining	
31	Rayburn <sup>19</sup>	M	2	Laryngeal diphtheria and empyema	Not stated	Partial resection left 5th and 6th cartilages	Died, 3 days after operation	
32	Attix <sup>20</sup>	M	55	Pneumonia (left)	<i>Pneumococcus</i>	Partial resection left 5th, 6th and 7th cartilages	Recovered	
33	Train <sup>21</sup>	M	7	Septicemia	<i>Staph aureus</i>	Epigastric approach (subcostal, in two stages)	Recovered	Multiple soft tissue and bone abscesses
34	Ross <sup>22</sup>	M	5	? "Influenza"	? <i>Haemophilus pertussis</i>	Epigastric approach (subcostal, in two stages)	Recovered	
35	Bigger <sup>23</sup>	M	28	Pneumonia	Type 8 pneumococcus	Resection left 4th and 5th cartilages	Recovered	
36	Guio <sup>24</sup>	M	9	Septicemia and osteomyelitis	<i>Staphylococcus</i>	Resection left 4th, 5th and 6th cartilages	Recovered	
37	Tizon and Leroy <sup>25</sup>	M	12	Pneumonia (left)	<i>Pneumococcus</i>	"Method of Prof. Marquis"	Died, 1 day after operation	
38	Finoey and Morgan <sup>26</sup>	M	15	? Pneumonia	<i>Pneumococcus</i>	Resection left 4th, 5th and 6th cartilages	Died, 19 days after operation	Developed empyema (right) 8 days after operation; autopsy showed anterior mediastinal abscess

with chemotherapy; there is even less reason to expect suppurative pericarditis, similarly treated,

TABLE 3 *The Antecedent Disease in the Reported and Collected Cases of Suppurative Pericarditis.*

ANTECEDENT DISEASE	No. OF CASES	RECOVERIES	DEATHS
Pneumonia	13	8	5
Pneumonia with empyema	7	5	2
Empyema	5	3	2
Osteomyelitis	1	0	1
Osteomyelitis and septicemia	2	2	0
Septic arthritis	1	0	1
Suppurative arthritis and septicemia	1	0	1
Metastatic abscesses (hip region and foot joint)	1	0	1
Tuberculous pericarditis	2	0	2
Influenza	1	1	0
Postoperative pneumonectomy for bronchogenic carcinoma and empyema	1	0	1
(?) Primary pericarditis	1	0	1
Stab wound	1	1	0
Ulcerative colitis and pyemia	1	0	1
Totals	38	20	18

to be cured. Nor is there any contraindication, as in acute empyema, to early open drainage.

The contrast of results in unoperated cases with those treated by pericardiostomy demonstrates that the latter offer a 50 per cent recovery rate, on the average, in collected series of cases. This is borne out in the most recently reported collected series of 99 cases by Shipley and Winslow,<sup>1</sup> in which 49 patients recovered. In the series of 38

TABLE 4 *Surgical Approach in the Reported and Collected Cases*

APPROACH	No. OF CASES	RECOVERIES	DEATHS
Anterior	29	16	13
Intercostal	1	1	0
Sternotomy	1	0	1
One cartilage and part of sternum	1	1	0
Two cartilages and part of sternum	1	1	0
One cartilage	6	4	2
Two cartilages	16	8	8
Three cartilages	3	2	1
Posterior	1	1	0
Epigastric	3	2	1
Two-stage epigastric and anterior	1	1	0
Not stated	4	0	4
Totals	38	20	18

cases considered here, there were 20, or 53 per cent, recoveries, although in the 10 reported cases only 4 patients survived. These results should be improved in the next few years with a wider use of chemotherapy in conjunction with pericardiostomy. It is generally agreed that nonoperative measures deserve no place in the treatment of suppurative pericarditis.

In considering the problem of pericardiostomy, one has a choice of several methods of approach.

**Intercostal approach.** This has been largely abandoned because of ineffectual drainage, inability to secure dependent drainage and the impossibility of exploring or visualizing the pericardial sac.

**Trans-sternal approach.** As early as 1648, Riolaus suggested trephining the sternum as a means of draining the pericardium. Winslow and Shipley<sup>32</sup> advocated this approach, but in a later communication<sup>1</sup> inclined to resection of the costal cartilages. The disadvantage of this approach is the limited opening through the unyielding sternum, even though a portion of sternum is rongeur away.

**Approach by resection of one or more costal cartilages, usually on the left.** This approach is the one most commonly employed, and usually includes the fifth and sixth cartilages—the third to eighth cartilages have been resected. The transversus thoracis muscle fibers are divided, and the left pleural leaf is wiped lateralward, exposing the pericardium, which is incised, and the cut edges are sutured to the fascia or skin. In this method, pocketing of pus may occur posterior to the heart, or the heart itself may tend to occlude the drainage opening, however, placing the patient in the prone position may improve drainage. Occasionally, the corresponding cartilages on the right are resected. This was done in one of our cases (Case 4).

**Xiphocostal or Larrey's angle approach, with resection of the seventh cartilage.** This was later modified by Ogle and Allingham<sup>33</sup> to make their epigastric approach, in which the peritoneum is stripped from the diaphragm, and the pericardium entered dependently. This method has not been widely used, and we have had no personal experience with it, but it is said to give excellent dependent drainage, although, with the patient lying on his back, it seems to be subject, and for much the same reason, to the difficulties encountered in drainage by resection of the cartilages.

**Posterior approach.** Loucks,<sup>34</sup> Moore,<sup>8</sup> Truesdale<sup>3</sup> and Andrus<sup>35</sup> have reported favorably on this method, which is designed to drain the pericardial sac in its most dependent portion when the patient is recumbent. This approach requires traversing the left pleural cavity, and if this is not obliterated by adhesions, as it was in the cases of the operators noted above, the additional load of empyema thoracis is imposed and must be dealt with. This need not be insuperable, but the impression persists that this approach may best be used as a secondary operation, if pleural symphysis is not present.

Table 4 shows the approaches used in the 38 reported and collected cases.

There is no unanimity of opinion regarding the use of drainage material once drainage has been

established surgically. All types of materials have been used without any preponderance of evidence in favor of one or another. It is undoubtedly important that the pericardial cavity be explored with the finger at the time of operation, and at any later time that pocketing may be suspected. In 3 of our patients (Cases 3, 4 and 5), it was necessary daily to pass the finger around the heart to break up completely the fibrinous adhesions that formed regularly for the first five postoperative days. The patient was not upset by this procedure and complained of pain only when the finger pressed the pericardium anteriorly against the deep surface of the sternum. Some authors have placed Dakin's tubing or another type of tubing posterior to the heart. This has seemed to us a dangerous practice, and this impression was substantiated by an accident that occurred during the convalescence of one of our patients (Case 3). Although we have used no drainage tubing in our 5 personal cases, in Case 3 we experimented with various types of irrigating and suction tubing placed at the wound edges and not within the pericardial sac. Owing to a misunderstanding, a piece of 8-mm. red rubber tubing was placed within the pericardium, so that it was in contact with the inferior aspect of the right ventricle, and allowed to remain in place for approximately twelve hours. This resulted in a deep, eroded groove in the substance of the ventricle in contact with the tube, with ensuing brisk hemorrhage from the vessels in the eroded myocardium. It was necessary to take the patient to the operating room, and to rotate the heart outward and to the left before two silk sutures could be placed to control the bleeding. Fortunately, convalescence was uneventful thereafter.

As a result of this experience, we are more firmly than ever of the opinion that drainage or irrigating tubes, placed and fixed within the pericardium, are a definite hazard.

We are completely in accord with those who have stressed the value of frequent irrigations. We have employed gravity flow from a height of not more than 50 cm. above the pericardium, directing the fluid to the posterior portion of the sac by means of a No. 14 urethral catheter inserted at the beginning and removed at the conclusion of each irrigation. We have used a liter of Dakin's solution every three or four hours while purulent drainage continues, and have noted no such reactions as were suggested by the experimental work of Beck.<sup>36</sup> It has been used with apparently beneficial results by others,<sup>33</sup> and we have observed clearing of the pericardial infection with its use, whereas infections in other

organs have persisted and the patient has gone on to die from sepsis (Case 4).

PROGNOSIS

After studying the documented cases with respect to age of patient, sex, type of approach and postoperative care of the wound, one can determine no apparent effect of these factors on the prognosis. Although it seems reasonable to assume that those patients operated on earliest stand in the most favorable prognostic light, there is no weight of evidence to bear this out either in these 38 cases, or in those previously recorded. Shipley<sup>37</sup> states that of the 7 patients who recovered in his series, all were operated on early. On the other hand, of the 5 fatal cases only 1 was a late case.

We believe that prognosis depends on, first, the condition of the patient relative to the antecedent disease—as we have stated above, if the pericarditis is but a part of a pyemia, the outcome is usually fatal—and, secondly, the virulence of the infecting organism and, as a corollary, the resistance of the host. All the common pathogens and many of the rarer ones have been reported as the causative agent of suppurative pericarditis. Table 5 shows the organisms mentioned in the

TABLE 5. *The Etiologic Agents in the Reported and Collected Cases.*

ORGANISM	NO OF CASES	RECOVERIES	DEATHS
Pneumococcus, Type 1	2	1	1
Pneumococcus, Type 2	2	2	0
Pneumococcus, Type 4	1	1	0
Pneumococcus, Type 5	1	1	0
Pneumococcus, Type 8	2	1	1
Pneumococcus, type not stated	8	5	3
Staphylococcus albus	2	0	2
Staphylococcus aureus	7	4	3
Staphylococcus aureus (hemolytic)	1	0	1
Streptococcus hemolyticus	1	1	0
Streptococcus nonhemolyticus	3	2	1
Germ of nature of colon bacillus"	1	1	0
"Appearance of B. pertussis"	1	1	0
Not stated	6	0	6
Totals	38	20	18

38 reported and collected cases. It appears from this that the pneumococcus, with 11 recoveries and 5 deaths, is the most benign of the invaders, since, of the remainder, there were 9 recoveries and 13 deaths. These assumptions are not borne out in the literature. Undoubtedly, with the newer chemotherapy one may expect an appreciable improvement in these figures.

CASE REPORTS

AUTHORS' CASES

CASE 1. C.S., a 48-year-old man, was admitted to the Third Medical Service of the Boston City Hospital on December 27, 1936. He gave a history of pneumonia of

4 days' duration. Physical signs of consolidation of the left lower lobe were present and were confirmed by roentgenogram. On December 31, 1936, a pericardial friction rub was heard over the entire precordium. On this day, also, the patient left the hospital against advice, and was apparently comfortable for a week. However, 1 week before re-entry on January 18, 1937, he began to have cough, fever, chills, sweats and pain in the left chest.

On physical examination, the heart was enlarged to percussion. There was a pulse deficit, and the sounds were distant and muffled. Later, pulsus paradoxicus and enlargement of the neck veins were observed, and the pericardial effusion was confirmed by roentgenogram. Pericardiocentesis was performed, and 440 cc. of thick, greenish yellow pus was removed. The venous pressure prior to pericardiocentesis was 260 mm. of water, afterward, 170 mm. The patient was afforded temporary relief, and the next day 520 cc. of pus was removed from the pericardium. On the following day, he was transferred to the Second Surgical Service for pericardiostomy, which was carried out under nitrous oxide and ether anesthesia. The left 4th and 5th cartilages were resected, and the pericardium was opened. About 700 cc. of thick, yellow pus was evacuated. The pericardium was sutured to the skin, no drainage material was used. Postoperatively, the pericardial sac was irrigated with warm saline solution.

The patient showed considerable improvement, but by the 7th postoperative day an empyema was noted in the left thorax, from which a hemolytic streptococcus was cultured. Thoracentesis was performed on 4 successive days, meanwhile, the condition grew progressively worse, bronchopneumonia developed, and 10 days after operation the patient died.

CASE 2 V T, a 13-year-old girl, was admitted to the Second Medical Service of the Boston City Hospital on December 14, 1938. The patient had been well until 3 days prior to admission, when she complained of severe pain in the lumbar region and frequent urination. At the time of entry, she was febrile, flushed and dyspneic.

Roentgenograms demonstrated right lower lobe consolidation. Throat cultures showed a Type 6 pneumococcus, in addition to *Staphylococcus aureus*, and 200,000 units of Type 6 antipneumococcus serum were administered. In addition, the patient received sulfanilamide and, later, sulfapyridine. On December 18, two blood cultures, which had been taken previously, yielded *Staph aureus*. In view of this, together with the failure to respond to serum therapy, it was thought that the patient had *Staph aureus* pneumonia and septicemia. She was given 200,000 units of Lederle's antistaphylococcus serum, and there was transitory improvement. On the 8th hospital day, a pericardial friction rub developed, and extension of the pneumonic process was noted. Three days later, the area of cardiac dullness increased, and a pericardial tap yielded 4 cc. of serosanguineous material. Culture showed *Staph aureus*. The patient was transferred to the Second Surgical Service, and pericardiostomy was performed on December 26. The 4th and 5th left costal cartilages were resected, and the pericardium opened. A small amount of pus and considerable fibrin were irrigated from the pericardial cavity. The pericardium was sutured to the skin, and no drainage material was inserted into the pericardial cavity. The pericardium was irrigated with warm saline solution.

Postoperatively, the condition continued to be grave, widespread bronchopneumonia with considerable pulmonary edema developed, and the patient died 42 hours after operation.

CASE 3 W B, a 33-year-old Negro laborer, was admitted to the Third Surgical Service of the Boston City Hospital shortly after having received multiple stab wounds of the chest on January 21, 1939.

On admission, he was in mild shock, and three stab wounds were noted, one over the midsternum, one in the region of the left 10th costochondral region, and one 2.5 cm. directly below the left nipple in the 5th left intercostal space from which there was moderate bleeding. Shock was relieved by heat, position, fluids and Coramine. The patient's progress was entirely uneventful until the 3rd hospital day, when he developed acute intestinal obstruction, for which laparotomy was performed under spinal anesthesia. The obstruction was found to be due to volvulus of the proximal ileum, and was relieved. The left leaf of the diaphragm was explored for evidence of injury, but none was found. There were no subsequent abdominal symptoms.

On the 8th day following entry, the wound beneath the left nipple, which had on occasion drained a small amount of bloody material, began to drain pus, and the patient became febrile. Cardiac enlargement, noted clinically, was later confirmed by roentgenograms. On February 11, examination showed—in addition to a chest wound draining pus—distended neck veins, paradoxical pulse, cardiac enlargement and a venous pressure of 170 mm. of water. The patient was transferred to the Second Surgical Service, and on February 12, under cyclopropane anesthesia, pericardiostomy was carried out. The left 5th and 6th cartilages were resected, the pericardium was opened, and approximately 1000 cc. of foul pus was aspirated. *Staph aureus* was obtained on culture. The cavity was irrigated with physiologic saline solution, and the edges of the pericardium were sutured to the skin. No drainage material was placed in the pericardium. The patient showed immediate improvement.

The day following operation, an irrigating catheter was placed midway in the right border of the wound, but was not allowed to pass within the pericardium, the over flow was taken care of by another tube placed at the wound edge and connected to continuous suction. This system functioned well and kept the pericardial cavity bathed in fresh solution, at first, saline and, later, Dakin's solution. On February 23, the position of the catheter was changed to the lower angle of the wound and, inadvertently, allowed to remain in contact with the inferior aspect of the right ventricle for about 12 hours. The constant action of the heart against the catheter eroded the myocardium of the right ventricle. Two days later brisk hemorrhage from a myocardial vessel in the substance of the right ventricle occurred. It was discovered immediately, and two fine silk sutures were placed so as to occlude the bleeding vessel. Following this, the patient's recovery was steady, and by May 10 the pericardial wound was completely closed. However, there remained a short draining sinus down to the left 6th cartilage near the costochondral junction. Since the pericardium was well covered by skin, this sinus was excised. It filled in completely after several weeks.

Shortly before discharge, on June 26, a roentgenogram showed the size of the patient's heart to be normal. An electrocardiogram obtained in September, 1939, was well within normal limits. The patient has been followed for 20 months since operation. He is well and working as a coppermith. There is no evidence of adhesive pericarditis or impaired cardiac reserve on normal activity.

CASE 4 H S, a 44-year-old woman, had had ulcerative colitis for 10 months prior to her admission to the Boston City Hospital on June 25, 1940. There had been

a weight loss of 20 pounds. She was treated medically until August 23, when an ileostomy was performed. Following this, she had a very unsatisfactory course, since she could not be kept in fluid balance and the albumin-globulin ratio was reversed, the total serum protein being 4.5 gm. per 100 cc.; the blood chlorides remained about 85 milliequiv. per liter.

On October 2, a pericardial friction rub with pericardial effusion was noted, and at the same time there was evidence of sepsis in the right eye. Pericardicentesis was performed, and seropurulent fluid was obtained in which staphylococci were seen on direct smear. Pericardiostomy was performed on October 3, at which time her condition was poor. The 5th and 6th left costal cartilages were resected, and the pericardium was opened. Between 500 and 700 cc. of thin, yellow pus, which showed *Staph. aureus* and *Staph. albus* on culture, was evacuated.

The patient improved somewhat following this, but she continued to have frequent bowel movements. Ulcerations perforated the right cornea, and pus drained from the eyeball. She also developed a rectovaginal fistula. There was a small bloody effusion in the left pleura from which *Staph. aureus* was cultured, but which was well localized by aspirations. It was necessary daily, for the first 5 postoperative days, to break up, with the finger, fibrinous adhesions that formed between the heart and pericardium. The patient failed and died on October 11.

Autopsy revealed no infection of the pericardium. There were a localized collection of blood clots in the left costovertebral pleural gutter, panophthalmitis of the right eye and generalized peritonitis, the result of the perforation of one of the ulcerations of the ileum.

CASE 5. J. P., a 15-year-old boy, was admitted to the Fourth Medical Service of the Boston City Hospital on October 15, 1940. He was desperately ill with a left-upper-lobe pneumonia of 2 days' duration, as demonstrated by physical signs and roentgenograms. Sulfathiazole therapy was begun, and a Type 5 pneumococcus was identified in the sputum. The blood culture taken on admission was also positive for Type 5 pneumococcus. There was definite improvement, but the temperature did not return to normal after 3 days.

On October 19, a pericardial friction rub was heard, and a roentgenogram showed definite pericardial effusion and also fluid in the left pleural cavity. There was marked pulsus paradoxicus. Pericardicentesis yielded no fluid, but the picture was so characteristic and the patient's condition so precarious that exploration of the pericardium was believed to be indicated, and he was transferred to the Second Surgical Service. Under local anesthesia, the 5th and 6th left costal cartilages were resected. Before the pericardium was opened, a needle was inserted and turbid straw-colored fluid obtained, which on direct smear showed numerous polymorphonuclear leukocytes but only questionable cocci. The left pleural lappet was fused and densely adherent to the pericardium, so that it was necessary to enter the pericardium by traversing the fused pleural layers. In so doing, no air was observed to enter the pleura, but a few cubic centimeters of fluid escaped. The pericardium, which was grossly thickened, was opened widely in the usual manner, and about 300 cc. of turbid fluid aspirated.

During the ensuing 2 weeks, many repeated cultures from the pericardium yielded Type 5 pneumococcus, although the cultures taken at operation were sterile. For the first 7 days, it was necessary daily to pass the finger around the heart to break up the fibrinous adhesions

that had formed. On October 31, after several thoracenteses, a portion of the left 8th rib was resected, and the Type 5 pneumococcus empyema drained. Following this, convalescence was uneventful. The pericardiostomy wound healed in 40 days. The electrocardiogram was within normal limits, the empyema cavity obliterated, and the patient was discharged from the hospital on December 14.

#### ADDITIONAL BOSTON CITY HOSPITAL CASES\*

CASE 6. W. P. B., a 30-year-old physician, was admitted to the First Medical Service of the Boston City Hospital on January 18, 1913. He had had pneumonia 18 months previously, and at the time of admission was prostrated, dyspneic and cyanotic. On the following day, signs of consolidation in the right upper lobe were noted. After 3 days of high fever and a rather toxic course, the temperature dropped sharply to normal and the lungs cleared.

On the 5th day after entry, a pericardial friction rub was audible, and the patient was again febrile. Three days later, signs of pericardial effusion were present, and by January 31, 1913, the effusion had increased, the pulse became irregular and paradoxical, and the patient continued to be febrile. On February 18, aspiration of the pericardium yielded thick, yellow pus, from which pneumococci were cultured. On the same day, he was transferred to the Third Surgical Service, and pericardiostomy was performed under ether anesthesia by the late Dr. E. H. Nichols. The pericardium was entered after resection of segments of the right 4th and 5th costal cartilages, and 300 cc. of thick, yellow pus evacuated. A rubber-tissue cigarette drain was inserted into the pericardial cavity.

The patient was markedly improved following the operation, and his temperature at once became normal. On March 26, 1913, a portion of necrotic rib was removed, following which the wound promptly healed.

The patient at the present time (December, 1940) is in good health and actively engaged in practice as a dermatologist. There are no cardiac symptoms.

CASE 7. S. E., a 17-year-old boy, was admitted to the Second Medical Service of the Boston City Hospital on November 27, 1917. Two weeks before entry, he began to have substernal and generalized pain throughout the chest, dyspnea, orthopnea and, later, chills, fever, sweating and anorexia.

On admission, the temperature was 102°F.; the patient was acutely ill, with a flushed face, but there was no dyspnea or cyanosis. At the base of the right chest posteriorly there was dullness, the breath sounds were diminished, and a few rales were heard. The liver was not enlarged, and there was no edema. The left border of the heart was 2 cm. beyond the mid-clavicular line in the 5th interspace, and the sounds were distant. The patient continued to be quite ill, and dyspnea and cyanosis developed.

Examination on November 30 revealed fluid at both bases, further increase in the area of cardiac dullness, and distant and muffled sounds; the liver was enlarged, and there was peripheral edema. On December 3, there was roentgenographic evidence of pericardial effusion. The patient continued to run a septic course and developed an irregular paradoxical pulse, the cardiac shadow increased in size, the cyanosis, dyspnea and peripheral edema increased, and ascites developed. On December 30, pericardicentesis was done, and 550 cc. of thin, greenish pus was obtained. The next day, pericardiostomy was per-

\*We are indebted to Drs. H. A. Bouvé, E. D. Churchill and H. B. Loder for permission to report the cases of the patients on whom they operated.

formed under ether anesthesia by the late Dr E H Nichols. A portion of the sternum and the 5th left cartilage were resected, and the pericardium opened. A rubber wick was inserted for drainage, and the wound was closed about the drain.

The patient was much improved by operation, and the pericardial wound drained profusely. He did well for 8 days, and there was a decrease in the amount of drain age. The wound became a small sinus, and completely closed on the 15th postoperative day. The patient then became irrational and edematous, developed bronchopneumonia, and died on the 28th postoperative day.

CASE 8 B C, a 14-year-old girl, was admitted to the Third Medical Service of the Boston City Hospital on August 15, 1921. Two weeks before entry, she had noted swelling, heat and tenderness of the distal phalanx of the right index finger, which discharged pus spontaneously. The patient was apparently well until 8 days before entry, when the right knee joint became painful, red and swollen. On admission, she appeared quite toxic. There were redness, swelling and tenderness in the distal phalanx of the right index finger, heat and swelling over the anterior portion of the right knee and marked tenderness on motion of the knee. The day following admission under gas oxygen anesthesia, incision and drainage of the abscessed right index finger and right prepatella bursa were carried out. Cultures of the pus from each yielded *Staph aureus*.

The patient continued to run a septic course and on September 22, enlargement of the cardiac area was noted and was confirmed by roentgenogram. The sounds were muffled, the pulse paradoxical, and there were compression signs in the left lung. Cyanosis, dyspnea, precordial pain, abdominal distention and free peritoneal fluid were present. The same day, pericardicentesis yielded 360 cc of thick, grayish green pus. The patient was markedly relieved following this, and on the next day, under ether anesthesia, pericardiostomy was performed by Dr H B Loder. Segments of the left 5th and 6th costal cartilages were resected, and the pericardium was opened. A rubber tube was inserted into the pericardium.

Postoperatively, the patient failed to improve, continued a febrile course with increasing ascites, and died 23 days after operation.

CASE 9 M S, an 18-year-old student, was admitted to the Fourth Medical Service of the Boston City Hospital on December 5, 1930. One week before entry, he began to feel sharp pains in the ensiform region, made worse on breathing and accompanied by fever, headaches and anorexia. On the day before entry, the chest pain became worse, and there were dyspnea and a nonproductive cough.

On entry, the chest findings were consistent with a moderate bilateral effusion, and the heart was enlarged. Thoracentesis was done, and 100 cc of slightly cloudy, yellow fluid was removed from the left chest. Cultures showed no growth. A febrile course continued, and on the 6th day, 450 cc. of similar fluid was removed from the left chest. On the 12th day, it was noted that the area of cardiac dullness was increased, and the pulse was paradoxical. At no time was a pericardial friction rub heard. At this time, there were definite signs of fluid in the right thorax, and thoracentesis yielded 1250 cc of slightly cloudy, yellow fluid from which no organisms could be cultured. On the 19th hospital day, fluid was again removed from the right thorax, and at this time the area of cardiac dullness was very definitely increased. This was confirmed by a roentgenogram, which revealed enlargement both to the right and to the left. On Decem-

ber 24, pericardicentesis yielded 20 cc. of yellowish purulent fluid. Smear showed no organisms, and culture revealed no growth. By that time, the patient was very much worse, dyspnea, orthopnea and cyanosis were increasing. Two days later, a pericardiostomy was performed by Dr E D Churchill, under local anesthesia. Segments of the left 6th and 7th costal cartilages were resected, and a very thick, fibrous pericardium exposed and opened. A large quantity of pus was evacuated. Cultures from this yielded *Staph aureus*. A tube was inserted just within the pericardium.

The patient experienced immediate relief, and his postoperative course was uneventful. He was discharged from the hospital on the 48th postoperative day, symptom free and with the wound healed.

CASE 10 F L, a 12-year-old boy, was admitted to the Pediatric Service of the Boston City Hospital on June 8, 1930. He gave a history of malaise, fever and chills.

The entire right chest showed flatness, decreased breath sounds and decreased vocal and tactile fremitus. A roentgenogram revealed uniform density of the entire right chest, with displacement of the heart and trachea to the left. On June 10 the empyema was drained by the intercostal closed method, and 1400 cc of pus was obtained from which a Type 1 pneumococcus was cultured. Following this procedure, there was some improvement, although the patient continued to be febrile.

On June 19, physical examination showed cardiac dullness extending into the left midaxillary region. The heart sounds were faint and indistinct. A diagnosis of pericarditis was made, and pericardicentesis on June 19 yielded pus containing Type 1 pneumococcus. On the same day, pericardiostomy was performed by Dr H A Boue. Under local anesthesia, a cartilage was resected and a catheter inserted into the pericardium through a trocar.

The patient failed to improve postoperatively, and died on the 15th day following operation.

#### SUMMARY AND CONCLUSIONS

Ten cases of suppurative pericarditis treated by pericardiostomy and hitherto unreported are presented.

Twenty-eight additional cases have been collected from the literature from January 1, 1934 to January 1, 1940, which, with the above 10 cases, brings the total of recorded cases to 265.

Suppurative pericarditis is not a rare disease, as is demonstrated by the autopsy figures.

The diagnosis is frequently missed, because the condition is obscured by concomitant thoracic disease.

In untreated cases, the mortality approaches 100 per cent.

With pericardiostomy, the treatment of choice, the mortality is 50 per cent.

With chemotherapy as a supplement to pericardiostomy, there should be a further reduction of mortality.

Pericardiostomy should be undertaken early to achieve optimal surgical conditions and probable further lowering of mortality. Such a policy may involve operating on a certain number of patients in whom the diagnosis cannot be proved by peri-

cardicentesis, and even in a few in whom organisms cannot be found in the fluid obtained by early pericardicentesis.

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## DYSPHAGIA AND NUTRITIONAL DEFICIENCY\*

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THE most significant causes of dysphagia are carcinoma and other malignant tumors of the esophagus, cardiospasm or achalasia of the esophagus, benign esophageal stenosis (or stricture), hypochromic anemia, with the Plummer-Vinson syndrome, and paralysis of the ninth or tenth cranial nerves. Dysphagia very rarely occurs in association with a dilated left auricle, pericarditis, a sacular aneurysm, a dissecting aneurysm or an anomalous aortic arch.<sup>1</sup> A certain degree of dysphagia may also be present in gastric diaphragmatic hernias, especially in those cases in which there is a congenitally short esophagus or in which the lower end of the esophagus is kinked as a result of hernia.<sup>2</sup>

Since cancer of the esophagus is one of the most inexorable forms of neoplastic disease and since most of the other conditions causing dysphagia are amenable to appropriate therapy, it is imperative to establish the etiology of a given case so that the proper treatment may be promptly instituted.

Recently, several cases have come to our atten-

tion that at first were thought to be cancer of the esophagus but on further study were found to have dysphagia apparently due to polyneuritis secondary to nutritional deficiency. An adequate diet, with vitamin supplements administered by mouth, by stomach tube or by gastrostomy tube, as the situation necessitated, resulted in amelioration of the polyneuritis and disappearance of the difficulty in swallowing.

This aspect of deficiency disease has rarely been stressed in this country, but seems to be sufficiently important to warrant serious consideration.

In 1924, Vinson,<sup>3</sup> reporting 415 cases of "cardiospasm," said that the etiology is unknown but "among the causes may be primary spasm, primary atony of the musculature of the esophagus, irritative lesions of the vagus nerves [*italics ours*], esophagitis, fissures of the cardia, kinking of the esophagus at the hiatus esophagi and extrinsic pressure from the liver."

In 1938, Carr and Vinson<sup>4</sup> considered cardiospasm to be due to either vagal hypoactivity or a sympathetic hyperactivity, or both, but they admitted that the underlying cause of the autonomic imbalance is unknown.

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Knight,<sup>6</sup> studying the physiology of the esophagus in cats, concluded:

(1) The esophagus receives a sympathetic innervation (2) There is a true intrinsic sphincter at the cardia (3) Vagal stimulation causes tetanic contraction of the upper one third of the esophagus, which is composed of striated muscle. This contraction is augmented by sympathetic stimulation (4) Vagal stimulation causes increased tonus and motility of the lower one third of the esophagus, which is composed of smooth muscle. The tonus and motility are inhibited by sympathetic stimulation (5) Bilateral vagal section reproduces the appearances of achalasia of the cardia. Simultaneous removal of the sympathetic fibres prevents the onset of this obstruction. When the obstruction develops it can be relieved by section of the sympathetic supply to the sphincter (6) The sympathetic supply of the cardiac sphincter is accessible as it passed to the sphincter along the course of the coeliac axis and left gastric arteries

Pollitzer<sup>6</sup> reported a case of marked esophageal dilatation in a sixty seven year-old woman who had had dysphagia for thirty years. Autopsy showed compression of the vagus nerves by enlarged mediastinal lymph nodes. He believed that pressure on the vagus nerves had caused dilatation of the esophagus.

Various authors<sup>7-13</sup> have reported pathologic findings in Auerbach's plexus in post mortem studies of cases with achalasia of the esophagus. Constant findings were degeneration of this nerve plexus and hypertrophy of the circular muscular layer of the esophagus. Occasionally, in addition, small collections of lymphocytes and plasma cells, which suggested a certain amount of chronic inflammation, were found scattered throughout the wall of the esophagus.

Lendrum<sup>13</sup> has pointed out that the loss of ganglion cells in Auerbach's plexus is as great in the undistended portion of the lower esophagus as in the distended portion. This fact suggests that the pressure associated with the distention is not the cause of the degenerative changes in the nerve plexus.

Looser<sup>14</sup> reported a case of cardiospasm with enormous dilatation of the esophagus in a twenty-one year-old woman whose symptoms dated back to diphtheria at the age of twelve. He mentions no paralysis in this case, and he effected a cure by forcible dilatation of the lower end of the esophagus after performing a gastrostomy.

In view of the present day knowledge of the significance of nutritional deficiency in the etiology of many types of polyneuritis, it is of great interest that Vinson,<sup>15</sup> reporting 186 cases of cicatricial (benign) stricture of the esophagus in 1927, noted the following etiologic factors: 18 cases had no obvious cause for stricture, 14 fol-

lowed typhoid fever, 13 followed severe vomiting of pregnancy, and the remaining 141 were accounted for by various caustics, congenital defects and infectious diseases. In other words, 27 cases out of 186 (14 per cent) developed following typhoid fever or pernicious vomiting of pregnancy, conditions that are now known to be frequently associated with manifestations of deficiency disease. Vinson does not, however, include sufficient clinical information to enable one to estimate the incidence of recognizable deficiency-disease syndromes among his patients.

Turner,<sup>16</sup> reporting on 19 cases of nonmalignant esophageal stenosis, found that 5 were due to ingestion of corrosives, 5 were congenital, 4 were due to acute inflammation, and in 2 the cause was undetermined. He also said that simple strictures have followed scarlet fever, typhoid fever and the vomiting of pregnancy, but offered no explanation of this unusual sequence of events.

Stinson,<sup>17</sup> in 1938, reported 4 cases treated and cured with thiamin chloride. He came to the conclusion that cardiospasm is a manifestation of vitamin B<sub>1</sub> deficiency, that vitamin B<sub>1</sub> given intramuscularly relieves certain types of cardiospasm, and that the continued administration of this vitamin prevents the recurrence of attacks. Unfortunately, his paper includes no histories of dietary deficiency, nor does he include descriptions of physical signs of the better known syndromes now accepted as being due to vitamin deficiency. From the evidence given, it is hardly justifiable to consider that he has proved the etiologic relation of vitamin B<sub>1</sub> deficiency to cardiospasm.

Meiklejohn<sup>18</sup> has recently cast some doubt on the experimental evidence usually quoted as proving that thiamin (vitamin B<sub>1</sub>) is actually the antineuritic vitamin, but he concedes the relation of dietary deficiency to certain neuritides.

Fenwick,<sup>19</sup> in 1893, published a paper discussing spasmodic stricture of the cardiac orifice of the stomach. He noted "Habitual drunkards are very liable to the complaint especially after indulgence in an unusually deep debauch. In many of these cases a bougie is only arrested in the immediate neighborhood of the stomach, but in others the obstruction is encountered just below the pharynx." He mentions one case in a youth with acute phthisis, and also says that dysphagia sometimes appears following an acute febrile illness. Of some historical interest is his comment that a mild form of the complaint is frequently encountered in emotional and anemic women between the ages of eighteen and thirty, in some cases making its appearance coincident with the establishment of the menses. Perhaps he refers here to two

conditions that would now be diagnosed as globus hystericus and idiopathic hypochromic anemia with the Plummer-Vinson syndrome.

Jankelson<sup>20</sup> reported 6 cases of dysphagia that were relieved by the administration of vitamin B. One of his patients had severe polyneuritis, another had paresthesias and weakness of the arms, and a third had pain in the calf muscles and marked general weakness. The others had no demonstrable neuritis. Four patients had no x-ray evidence of disease in the esophagus or stomach, one had a small diverticulum in the middle third of the esophagus, and the sixth case had no x-ray studies reported.

Manson-Bahr,<sup>21</sup> in discussing the nerve lesions of beriberi, says that the cranial nerves above the seventh are rarely involved, but in some cases the laryngeal muscles are paralyzed. In the infantile form of beriberi, laryngeal paralysis is believed to be relatively common, and dysphagia and aphonia may be present.

Vedder,<sup>22</sup> discussing the pathology of beriberi, states that degenerative changes are found in the posterior columns as well as in the anterior and posterior nerve roots and ganglion cells. He adds, "It is especially to be noted that degeneration of the sympathetic system has been demonstrated, as in branches of the cardiac plexus, the splanchnic nerves and branches of the solar and renal plexus."

Laryngeal symptoms have been reported in beriberi by Fernando,<sup>23</sup> and paralysis of both recurrent laryngeal nerves in beriberi by Miura.<sup>24</sup>

Etzel<sup>25</sup> and Netto<sup>26</sup> believe that achalasia of the pylorus in the adult is identical in etiology and pathologic physiology with megaesophagus (achalasia of the esophagus), hypertrophic pyloric stenosis in the newborn, and megacolon, these conditions being due to vitamin B<sub>1</sub> deficiency. The pathology in all is the same and consists in marked diminution of elements of Auerbach's plexus.

Brodie,<sup>27</sup> in some experimental work on rats on the etiology of congenital pyloric obstruction, was able to produce this condition in 10 out of 23 young rats (four litters) by keeping the mother's diet minimal in antineuritic vitamin (B complex). The vagus nerves of the affected rats showed myelin degeneration.

The preceding observations suggest that dietary deficiency may be a cause of dysphagia, although the mechanisms involved may vary.

Iron-deficiency anemia associated with dysphagia causing the Plummer-Vinson syndrome has been so frequently reported that no further mention of it will be made here, even though the mechanism

by which the dysphagia is brought about is anything but clear.

The following 3 cases are reported as examples of dysphagia secondary to nutritional deficiency.

### CASE REPORTS

CASE 1 (formerly reported by one of us [D.M.<sup>28</sup>]). R. W. (P. 7094), a 55-year-old laborer, was transferred from a large teaching hospital with a diagnosis of carcinoma of the esophagus. Two and a half months before admission, he developed a rapidly progressive dysphagia and became barely able to swallow liquids. During the same period, he lost weight and developed a generalized weakness of all the muscles, particularly of the hands and feet, associated with tingling and numbness during the last 4 weeks. He had been studied in the neurologic division of the other hospital, and diagnoses of cancer of the esophagus (on the basis of fluoroscopic examination), toxic paralysis of the 10th cranial nerves, and toxic myelitis had been made. The diagnosis of 10th-nerve paralysis was based on hoarseness, regurgitation of fluids through the nose and weakness of the left side of the palate.

The past history included exposure to tuberculosis 5 years before admission. The patient had worked for many years handling bags of lime in a very dusty atmosphere. For 5 years, he had had a "cigarette cough." He had been a heavy drinker of alcoholic beverages since the age of 14.

On examination, the positive findings were dullness, increased tactile fremitus and fine crackling rales over the right chest posteriorly. There was generalized atony and wasting of the large calf and thigh muscles and intrinsic muscles of the hands. The deep tendon reflexes were absent, the abdominal and cremasteric reflexes barely perceptible. There was slight diminution of vibration perception over both legs below the knees, and moderate tenderness to pressure along the deep nerve trunks in the thighs, calves and arms. There was a definite tendency to bilateral foot drop.

The significant laboratory findings were a red-cell count of 2,730,000 with a hemoglobin of 56 per cent (Sahli), and a white-cell count of 11,500 with a normal differential.

X-ray examination of the chest showed dullness of the upper half of the left lung and upper third of the right lung, which was interpreted as being due to tuberculosis or to metastatic carcinoma. Fluoroscopy of the esophagus showed a deformity of the first portion, without marked obstruction, and was thought to represent a large tumor projecting into the lumen of the pharynx. Studies repeated 2 weeks later showed no change. Laryngoscopy under general anesthesia showed a markedly thickened fold of mucous membrane that had the appearance of a web just behind the larynx. No ulceration was seen, and a No. 18 bougie passed readily through the esophagus.

Because of the evidence of polyneuritis and a history of alcoholism, the patient was started on a high-vitamin diet, with liver extract intramuscularly as a source of vitamin B. Although bedridden for 3 weeks after admission, he improved steadily so that he was able to stand and walk a little by the end of the 4th week. Then, because he was much stronger, esophagoscopy was performed but no disease was found; this was repeated and again was negative. It was also noted at this time that the patient could swallow even solid foods without difficulty.

Six weeks after admission, another x ray film of the chest was taken. The entire right lung was clear, only a few increased markings persisting at the left apex. The blood showed only slight improvement, in spite of liver and iron therapy. The red-cell count rose to slightly over 3,000,000, and the hemoglobin to 65 per cent.

During the 8th week, the patient developed an acute respiratory infection, with signs of congestion in both lungs. He became unco-operative, drowsy and confused. Neurologic examination and lumbar puncture were negative except for absent tendon reflexes, which had never returned. The course was then rapidly downhill. The patient developed what was thought to be a bronchopneumonia and died 12 weeks after admission.

A postmortem examination revealed multiple abscesses in both lungs, terminal bronchopneumonia, a normal esophagus and a cystic tumor of the right frontal lobe which on microscopic examination proved to be a fibrillary astrocytoma.

It is interesting that normal esophageal function as demonstrated by x ray and esophagoscopy returned while the patient was receiving large amounts of vitamin B complex, although he was suffering from a brain tumor and multiple lung abscesses that eventually caused his death.

CASE 2 E A (P 16023), a 66-year-old man, was admitted because of progressive dysphagia of 3 weeks duration. He had been an inmate of a state institution for 4½ years, with a diagnosis of manic-depressive psychosis. The throat trouble began as a sore throat, but difficulty in swallowing soon progressed to the point where even fluids were regurgitated through the nose. The patient had lost 20 pounds in the previous 2 months.

Physical examination was essentially negative except for dental caries and external hemorrhoids. Nutrition appeared to be excellent.

Because the patient was totally unable to swallow a gastrostomy was performed. Postoperatively, he did extremely well and gained weight rapidly. However, about 1 month after operation he complained of tingling of his hands and feet, his gait was unsteady, and he lost all position sense in his legs. His tongue was noted to be atrophic. Esophagoscopy revealed only a slight constriction about 25 cm from the teeth, with no evidence of cancer, although a barium swallow was promptly regurgitated and spilled into the trachea.

On gastrostomy feedings with added liver, sensation in the extremities returned, the gait became normal, and the patient was able to swallow liquids without difficulty. He was discharged back to the state institution 2 months after operation, with a diagnosis of esophageal spasm and stricture. He returned to the Out Patient Department 5 weeks later for a check up examination, at which time he was able to swallow solid foods without any trouble. The tongue was normal, but the knee jerks and biceps reflexes were absent. There was also a fine scaling desquamation of the extensor surface of the shins and forearms. A diagnosis of vitamin B deficiency, with polyneuritis and paralysis of the 10th nerve, was made, and brewer's yeast (four 7½ gr tablets after each meal and at bedtime) was prescribed.

The patient was seen again 1 month later, at which time he had gained 11 pounds and was able to eat any thing without difficulty, there was marked improvement of the paresthesia of his hands and feet. As he described it, he was able to wind his watch and know what he was doing. All evidence of dermatitis had disappeared, and the deep tendon reflexes, although sluggish, were present.

Esophagoscopy was repeated, and since no lesion was found, the gastrostomy was allowed to close.

The patient was last seen 7 months later, 11 months after the gastrostomy had been performed, he had gained another 4 pounds and had no symptoms or signs of any residual neuritis, and no symptoms referable to his esophagus.

In retrospect, it seems likely that the extensive neuritis and loss of 20 pounds of weight had been caused by the patient's failure to eat adequately during a depressed phase of his manic-depressive psychosis.

CASE 3 J W (P 10181), a 48-year-old man, was first seen in December, 1935, because of hoarseness of 4 months' duration, gnawing epigastric distress, increasing weakness and tingling, and numbness and coldness of the arms and legs. He had been able to take only milk and coffee and had had marked anorexia for the same length of time. He admitted excessive indulgence in alcohol for many years. Thirty-three years prior to admission, he had had an operation on his stomach, and 28 years later he had had an operation for ulcer of the stomach.

The striking findings on examination were marked hoarseness and inability to stand or walk without assistance. Neurologic examination showed hyperactive but equal knee and ankle jerks, and marked muscular weakness, efforts made to stand up resulted in clonic contractions of the leg muscles.

Laryngoscopy showed the vocal cords to be a little sluggish in motion, and there was a small tumor at the base of the epiglottis. A biopsy of this tumor showed only chronic inflammation.

The patient was placed on a high vitamin diet, with marked improvement of the neuritis. His appetite was excellent, he was able to swallow without difficulty, his hoarseness disappeared, and he was able to walk without support, though unsteadily, when he was discharged 1 month after admission. The final diagnosis was polyneuritis due to nutritional deficiency secondary to chronic alcoholism.

The patient was next seen again about 1½ years later, when he came to the Out Patient Department because of pain in the hypopharynx, difficulty in swallowing and hoarseness. Laryngoscopy showed marked congestion of the entire hypopharynx but no cancer. In December, 1939, after an interval of almost 2½ years, the patient was admitted from a state prison because of constant burning pain in the epigastrium, pain in the left lower quadrant of the abdomen and burning pain in the suprasternal notch. For the previous 2 years, he had been unable to eat anything except liquids and soft foods. For 14 months, he was at a veterans' hospital, where in June, 1939, because of inability to swallow, a gastrostomy had been performed. Although the gastrostomy had closed over, the patient had apparently gained 33 pounds in 6 months and could swallow better than before the operation. For the previous 12 months, he had been receiving hypodermic medication at 4-hour intervals because of abdominal pain. He had been in bed practically the entire time because of weakness. He could not lie flat in bed, however, because his throat filled up with mucus when he did.

Physical examination was surprisingly negative, considering the dramatic history. The liver edge was palpable 3 fingerbreadths below the costal margin. There were coarse tremors of the tongue and of all extremities. The knee and ankle jerks were equal and hyperactive. Gastrointestinal studies, including a barium meal and enema, were negative for any evidence of neoplastic disease. The blood Hinton reaction was negative. On a

high-vitamin diet containing brewer's yeast (six 5-gr. tablets after each meal and at bedtime), the patient improved rapidly, and was soon able to sit up and to walk when supported. He gained another 6 pounds in the 3 weeks at the hospital, and was discharged with no difficulty in swallowing and complete relief of the burning in the suprasternal notch, epigastric discomfort and left lower-quadrant pain. His strength was returning rapidly, but he still had marked muscular inco-ordination in his legs.

The discharge diagnosis was the same as that on the first admission to the hospital: polyneuritis due to nutritional deficiency secondary to chronic alcoholism. The dysphagia and aphonia were apparently due to involvement of the 9th and 10th cranial nerves by the polyneuritis.

### CONCLUSIONS

Dysphagia is occasionally a result of neuritis involving the ninth or tenth cranial nerves, which in turn is produced by nutritional deficiency, particularly of the vitamin B complex.

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## LEFT-SIDED PAIN IN BILIARY-TRACT DISEASE\*

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THE pain of biliary-tract disease is primarily epigastric or right-sided. Occasionally, however, there is a left-sided component in the pattern of pain reference. When this happens, either pancreatitis or an extension of the pericholecystic inflammation to the left side is generally a sufficient cause. However, pain only on the left side may occur in biliary-tract disease in the absence of an inflammatory process. In such cases, which are rare, the origin of the pain in the biliary tract may be overlooked because of the clinical habit of regarding the latter as possessing an exclusively right-sided innervation. On embryologic grounds, the common duct must be assumed to have a bilateral innervation. This provides a reasonable explanation for some cases of bilateral pain in noninflammatory disturbances of the biliary ducts and for the occasional case in which there is an exclusively

left-sided reference. This is not a new observation, but two striking clinical illustrations are recorded herewith to emphasize it and thus to minimize the likelihood of a misinterpretation of the existing disease in similar cases.

### CASE REPORTS

CASE 1. A 45-year-old woman was admitted with a history of severe stabbing pain of 8 years' duration, starting in the epigastrium and radiating around the left costal margin and to the left scapula. During the more intense seizures, pain was also felt in the left shoulder and arm, spreading to the finger tips. The onset of attacks bore no relation to the ingestion of food, to the kind of food, to bowel, bladder or catamenial functions, to rest or to exercise. The pain, instead of immobilizing her, caused her to roll about in bed; it was not colicky, but rather constant, lasting from 30 minutes to 12 hours. It was not relieved by food or alkalis. There was no nausea or vomiting. Six years before entry, following an attack in which slight jaundice was noted, a cholecystectomy was performed in another hospital. The gall bladder contained numerous stones and gravel. The surgeon's note was as follows: "A moderately thickened and enlarged gall bladder was adherent to the whole length of the

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duodenum. The common-duct and cystic-duct regions were explored and examined. The gall bladder was removed. The common duct was negative and was not drained. The pancreas was normal.<sup>11</sup> Following operation, the patient had attacks of acute pain in the chest, which were diagnosed as angina or pseudo-angina by a consultant. When last seen by him 1 year after the operation, she was still having severe attacks of pain, cutting off her breath,<sup>12</sup> and the consultant was not certain what the diagnosis was.

The patient was admitted to this clinic 6 years after the cholecystectomy. She stated that 10 days after the cholecystectomy she had an attack of pain exactly like those preceding the operation. The attacks continued as frequently and as severely as ever, but during the previous few years there had been no radiation of pain to the left scapula and left upper extremity. The pain began just below the xiphoid process, radiated along the left costal margin and caused difficulty in breathing. Following the seizures, she felt a girdlelike, squeezing sensation, which slowly subsided. There was no nausea or vomiting and no other symptoms referable to the gastrointestinal system. No jaundice was noted at any time. Amyl nitrate occasionally relieved the pain, often it did not. Between attacks there was no intolerance of food, heartburn, flatulence or constipation, the appetite was normal. There had been an attack of pain almost daily for the 2 weeks preceding admission.

Physical examination on admission was not remarkable except for the scar of the incision in the right upper quadrant and another of an appendectomy done when the patient was 16.

The stools, blood and urine showed normal findings. The icteric index was 6, and the blood Hinton and Kahn reactions were negative. Gastric analysis gave normal findings, the spinal fluid and the sugar tolerance curve were normal, and the electrocardiogram was negative. Radiologic study of the genitourinary tract, chest, spine, stomach and intestine gave findings within normal limits. Duodenal intubation yielded crystals of calcium bilirubinate and others suggestive of cholesterol. Accordingly, the patient was explored, with a preoperative diagnosis of cholelithiasis. After old adhesions in the region of the gall bladder bed had been freed, the common duct, which was slightly dilated and thickened, was opened and a single pea-sized gallstone found and removed from the lower end.

The patient recovered uneventfully and has been entirely symptom free, enjoying excellent health ever since, a postoperative interval of 2 years.

**Comment.** The exclusively left-sided radiation of pain, in the absence of jaundice, nausea, vomiting or other symptoms that might have suggested a diagnosis of cholelithiasis, was so misleading that no physician suggested the possibility of residual stone in the biliary tract until after 6 years of continued disability.

**Case 2.** A 71-year-old woman entered the hospital because of pain, colicky in nature, radiating around both costal margins and to the interscapular area in the back. A week before entry, she experienced her first attack, in which the pain was in the right upper quadrant and radiated to the back between the scapulas. In the second attack, lasting 9 hours, which occurred on the day of admission, the pain was more pronounced on the left side, but it radiated to both sides, giving her the feeling of a rope being tied around the waist.<sup>13</sup> She found no relief in any position. There was some nausea, but no vomiting. There was no history of chills, fever or jaundice. The patient had been treated for 2 years for attacks of sub-

sternal distress, pain in the left shoulder and dyspnea on exertion. These were attributed to coronary heart disease.

On admission, physical examination revealed tenderness and spasm in the right upper quadrant of the abdomen. The electrocardiogram showed sinoauricular bradycardia (rate, 55), left axis deviation, widened QRS complexes and probable intraventricular block. The urine contained a few red and white cells per high power field, and the blood white cell count was 8900. The icteric index was 15. A Graham test showed cholelithiasis.

For 6 days preceding operation, the patient had nightly seizures of bilateral girdle pain, of equal intensity on both sides. Cholecystectomy and common duct exploration were then performed. A small gall bladder containing numerous stones was excised, and several stones were removed from a dilated and thickened common duct. Tube common-duct drainage was established. There was no pancreatitis or evidence of an acute inflammatory process in the upper abdomen.

The convalescence was smooth until the 8th postoperative day, when clamping of the T tube caused severe discomfort, which was quickly relieved by unclamping the tube. Two days later a cholangiogram showed a residual common duct stone. In view of the patient's age and cardiac condition, further surgery was deferred. She was discharged with the T tube in place.

When seen 7 weeks later, she looked well. She stated that about 100 cc of bile came out of the tube in each 24 hours. She had been entirely free of all symptoms including the precordial pain attributed preoperatively to the coronary heart disease, although she acknowledged that exertion, the usual preoperative cause of the pain, had been avoided. Before operation, however, there had been some spontaneous pain in the left chest, which had not recurred since. To establish a possible relation between the common duct stone and the left-sided pain of which she complained in the immediate preoperative period, 30 cc. of physiologic saline solution was injected slowly into the T tube. She complained immediately of pain along the left costal margin and pain in the back below the angle of the left scapula. This procedure was repeated using 45 cc of saline injected rapidly, with the reproduction of the same pain in the same area. There was no pain reference whatever to the epigastrium or to the right side. The saline solution in both instances did not return to the through tube and therefore presumably passed by the stone and entered the duodenum. Incidentally, this procedure succeeded in forcing the stone into the duodenum, since a subsequent cholangiogram showed no stone. The tube was removed, and the patient has remained well to date.

**Comment.** This is a clinical experience demonstrating beyond doubt that distention of the common duct can cause exclusively left-sided pain. It behooves the physician not to dismiss the common duct from consideration in the differential diagnosis when the presenting symptom is pain in the left upper quadrant.

### SUMMARY AND CONCLUSIONS

In two patients with stone in the common duct, pain was referred only to the left side in one and to both sides with equal intensity in the other. In the latter case, distention of the common duct postoperatively produced pain on the left side only.

Common-duct obstruction, therefore, may cause pain referred only to the left side and in the ab-

sence of other signs or symptoms suggesting disease in the biliary tract. It is not always necessary to assume the presence of pancreatitis or some

other inflammatory process spreading to the left of the mid-line to explain left-sided pain in disease of the biliary system.

## ANTHRAX\*

### Report of a Case Treated With Antiserum and Sulfathiazole

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ALTHOUGH satisfactory progress has been made in the treatment of anthrax, this disease continues to be a serious industrial hazard. The greatest number of cases occurs among tannery workers, but those among wool handlers and agricultural workers are not far behind. Although the fatalities are lessening in a few states,<sup>1</sup> the general mortality shows no tendency to decline, in spite of the fact that effective treatment is available.

Anthrax has been known since ancient times, mention being made in the Bible and by authors such as Homer, Seneca and Ovid. Although the descriptions reveal that even at that time the transmissibility of the disease to man by the fur and wool of diseased animals was known, it was not until 1823 that Barthelemy proved its contagious character in animals.<sup>2</sup> Pollender, in 1849, was the first to observe organisms in the blood of animals with anthrax.<sup>3</sup> In 1850, Davaine and Rambert demonstrated experimentally the relation of anthrax to the malignant pustule.<sup>3,4</sup> This work was confirmed by Koch in 1876 and Pasteur in 1877.<sup>3,4</sup> It was with the aid of the new methods devised by Koch that a firm foundation was laid for further investigation of the etiology and spread of anthrax.

Anthrax is a specific, virulent, infectious disease, caused by the *Bacillus anthracis* and occurring in man in three forms<sup>2,5-7</sup>: the cutaneous, the pulmonary and the intestinal. The disease is communicable to man by contact, inhalation or ingestion of material infected with anthrax. The cutaneous form, also known as "external anthrax," is further subdivided into the malignant-pustule type and malignant anthrax edema. The intestinal and pulmonary types are also called "internal anthrax."

By far the commonest type is the cutaneous infection, usually occurring as the malignant pustule.

The typical malignant pustule is a single lesion beginning with intense itching at the point of inoculation, or a burning sensation followed by the appearance of a small red papule, which within twelve or fifteen hours becomes vesicular, the vesicle showing a central depression containing brownish fluid and surrounded by a slight edematous areola. The vesicle then dries, leaving a dark-brown eschar surrounded by a number of minute silvery vesicles. The tissue about the site of inoculation becomes swollen, owing to anthracomucin, and consists of a doughy, indurated, pinkish, edematous mass. The surrounding lymph nodes are generally swollen, painful and covered by edematous skin. It should be noted that a characteristic feature of the pustule itself is the absence of pain in and about the lesion. Even when the lesion is extensive, the patient may complain of only a sense of weight and slight tenderness on pressure, or a feeling of tightness because of swelling. The surrounding vesicles then become filled with hemorrhagic fluid, and the edematous area is infiltrated with blood and sometimes undergoes gangrenous degeneration. If the infection becomes generalized, all the symptoms of collapse eventually set in, the patient becomes pulseless, and respiration ceases.

Internal anthrax occurs far less commonly, intestinal anthrax being the rarest form. The pulmonary type is brought about by the inhalation of dust impregnated with anthrax bacilli, and is usually seen in woolsorters; there are pain in the chest, cough, expectoration of bloody sputum, and cyanosis. The intestinal type is usually produced by the ingestion of spores, and the symptoms of the disease are referable to the pulmonary and intestinal tracts. In the intestinal form, there are abdominal pain, nausea and vomiting and diarrhea. The constitutional symptoms of internal anthrax are severer than those in the simple malignant-pustule form.

The diagnosis of anthrax can be made only after all the criteria have been considered. A history

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of exposure to infection, followed by a physical examination presenting the clinical picture of anthrax, does not relieve the physician from performing bacteriologic tests that confirm the diagnosis. One must make a direct examination of the pustular secretion in the malignant-pustule form, of the sputum in pulmonary anthrax and of the feces in intestinal anthrax. Furthermore, only a positive stained smear is decisive. If the direct examination is negative, a culture should be made or a guinea pig should be inoculated before making a diagnosis including or excluding anthrax.

When the diagnosis of malignant pustule has been made, the question of therapy arises. It has been shown by recent experience<sup>8-10</sup> that any form of operation or cauterization is to be avoided, for such procedures permit the entrance of infectious material into the general circulation because of the severance of blood vessels and lymph channels, thus precipitating septicemia. It is known that the pustule of cutaneous anthrax often heals completely if no local interference is offered, and Didié<sup>11</sup> reports good results from the use of small doses of x-ray.

The accepted local treatment consists in thorough cleansing of the lesion with physiologic saline solution, absolute rest and immobilization of the affected part and the injection of antianthrax serum subcutaneously at four points fairly equidistant from the lesion, as advocated by Symmers<sup>12</sup> and by Regan.<sup>13</sup> These injections form an isolating barrier against anthrax bacilli, and should be repeated at intervals of four or six hours until the lesion is free of bacilli. The amount of serum to be used depends on the severity of the local inflammation. The lesion should then be covered by sterile gauze. Every cutaneous anthrax lesion is to be regarded as a potential generalized infection, and an intravenous injection of 150 to 200 cc. of antianthrax serum should be given, due care being taken that the patient is not sensitive to the serum. If the blood culture is found to be negative, no further intravenous injections are necessary. If one errs, it is thus on the side of safety, for valuable time is saved in the event of septicemia.

For the treatment of cutaneous anthrax with septicemia, in addition to local therapy, as described above, repeated intravenous injections of antianthrax serum are recommended. Favorable results have been reported from the use of relatively small doses of serum; however, as stated by Symmers<sup>12</sup>: "... it would appear that to depend upon the lesser quantities as a routine measure is sooner or later to court disaster—and in

dealing with a disease so treacherous as anthrax, it is well to leave a wide margin of safety." A proved, efficient therapeutic method for treatment consists in the immediate administration of 200 cc. of serum, repeating this in four hours, and then giving 50 cc. every four hours until the blood culture is negative. Nilsson<sup>14</sup> noted no difference in the therapeutic value of serum manufactured for human use and veterinary serum. Because of favorable results obtained by the use of organic arsenicals,<sup>15, 16</sup> these drugs may be employed as adjuvants to serum or as the main therapeutic agent if serum is not obtainable. The organic arsenicals, if used, should be given in one or two large doses. Small doses do not appear to have sufficient therapeutic effect to justify their use, and their cumulative effect is probably as dangerous as that of one or two large doses.

#### CASE REPORT

A 40-year-old man was admitted to St. Joseph's Hospital on September 7, 1940, with an anthrax pustule on the flexor surface of the left forearm at the level of the junction between the middle and the distal thirds of the radius. A dark-brown eschar, measuring about 2.5 cm. in diameter, was surrounded by a number of vesicles filled with hemorrhagic fluid. About 3 cm. from the eschar were two bullae filled with a brown serous fluid. The skin from the level of the middle part of the humerus to the fingers was markedly edematous, indurated, doughy and pink. The tissue in the edematous area revealed discrete pinpoint areas of hemorrhagic infiltration. Except at the time of injury, there was no complaint of pain, although the patient noted a feeling of pressure and numbness. The infected arm was about twice the size of the right arm. The axillary nodes were tremendously enlarged. The temperature was 100.2°F., the pulse 92, and the respirations 24; the white-cell count was 20,400.

The patient stated that 9 days before admission, while handling wool, he stuck a burr into the anterior surface of the left forearm. Except for slight itching in the inoculated area, there was no disturbance. The following day, he noticed a "burning sensation" and the appearance of an "area of redness." On the same day, a "pimple" developed, from which he squeezed pus. On the 3rd day, the surrounding skin began to "swell, and became hard and stiff." The swelling continued, and the hand and arm became so large that the patient sought medical advice.

At the time of admission, stained smears from the contents of the pustule and vesicles showed staphylococci but no evidence of anthrax bacilli. Agar plates inoculated directly from the pustule revealed staphylococci. A blood culture showed growth, and stained smears revealed gram-positive bacilli having the characteristic appearance of anthrax bacilli. Stained smears were again made from the contents of the vesicles; they showed anthrax bacilli. An emulsion was made, using one of the colonies on a blood-agar plate. Twenty-nine hours after the injection of 0.5 cc. of the preparation into the subcutaneous tissue of the abdominal wall of a guinea pig, the animal died. Necropsy showed a gelatinous infiltration of the superficial structures of the abdominal wall. The liver and spleen were markedly enlarged and congested. The suprarenal glands consisted of two large hemorrhagic cysts.

The kidneys showed pinpoint hemorrhagic areas. A stained smear of the free peritoneal fluid revealed the presence of anthrax bacilli, as did smears from the liver, spleen and suprarenal glands. Anthrax bacilli were grown in pure culture from the heart's blood and the suprarenal glands.

The patient was put to bed with the arm at absolute rest and in an elevated position. Staphylococci having been reported on the smears and culture, 2 gm. of sulfathiazole was administered at once. This amount was repeated in 4 hours, and then 1 gm. every 4 hours was given. Twenty-four hours later, when the blood culture revealed anthrax bacilli, antianthrax serum was administered; 150 cc. of serum was injected intravenously, and 50 cc. was injected subcutaneously at several points about the lesion. Six hours later, 200 cc. of serum was given intravenously, and 50 cc. was injected deep into the muscular tissue in the upper arm at the level of the upper and middle thirds of the humerus and again around the lesion. Six hours later, another 200 cc. of serum was injected intravenously. The amount was then cut to 100 cc. intravenously and 50 cc. about the lesion, given at 6-hour intervals. A total of 850 cc. of serum was administered in a period of 18 hours. Blood cultures taken the following morning, 17 hours after the beginning of antianthrax serum therapy, revealed the presence of anthrax bacilli. Twenty-four hours later, cultures and smears were reported negative for bacilli. Thus, after 14 days of illness, 24 hours of antianthrax serum and sulfathiazole therapy produced negative smears and cultures. Pending the report of another blood culture, 100 cc. of serum was given every 8 hours. Blood cultures and smears from the site of inoculation continued to be negative. Serum was omitted, but sulfathiazole was continued until September 16. The sulfathiazole level on September 15 was 5.1 mg. per 100 cc. A total of 1150 cc. of serum was given.

During the illness, the temperature varied from 98 to 102°F. The white-cell count fluctuated between 20,300 and 10,400. The blood smears and blood chemical findings were not remarkable. It is to be noted that 12 hours after the deep intramuscular circular injection of serum in the upper arm, a linear demarcated area of pinpoint hemorrhages was seen. Neither swelling nor dermal changes occurred above the injected area. Except for slight serum sickness, which was controlled by calcium gluconate and epinephrine in oil, the patient made an uneventful recovery and was discharged cured.

This case demonstrates the beneficial effects of massive doses of antianthrax serum. However, since staphylococci were found on smears and in cultures, sulfathiazole was administered. In view of the facts that the most beneficial effects are

obtained when antianthrax serum is used early, that late administration, even in massive doses, shows discouraging results and that, in this case, the serum was given effectively late in the course of the disease, the question is, Does sulfathiazole act synergistically with serum? In-vitro experiments performed on six different occasions showed that anthrax bacilli grew less readily on plates containing sulfathiazole powder and antianthrax serum than they did on plates containing sulfathiazole or serum alone. Although these experiments do not prove conclusively that sulfathiazole is an effective adjuvant, the results serve as a basis for further experiment.

### SUMMARY

The modern diagnosis and treatment of anthrax are discussed.

A case successfully treated with antianthrax serum and sulfathiazole is reported, and the possible value of the latter as an effective therapeutic adjuvant is considered.

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## MEDICAL PROGRESS

## THORACIC SURGERY

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## BRONCHIAL ADENOMA

IN last year's review,<sup>1</sup> attention was called to the discrepancies that may occur in end-result statistics purporting to deal with primary bronchogenic carcinoma by different interpretations of the nature of the so-called "bronchial adenoma." There are now sufficient definitive characteristics on record to permit the recognition of this tumor both clinically and pathologically in nearly every case. Only occasionally is the small fragment of tissue obtained by bronchoscopic biopsy inadequate for an unmistakable histologic diagnosis. If certain controversial aspects of these tumors are avoided, there seems to be general agreement on the following characteristics:

*Slow rate of growth.* Not infrequently, there is direct proof from symptoms, radiography or bronchoscopic biopsy that the tumor has been present five years or longer and still remains small and sharply circumscribed.

*Early age incidence.* Approximately four fifths of the reported cases occur before the age of forty.

*Relatively equal sex incidence.* Several series of cases indicate that the tumor occurs in females with a frequency as great as or even greater than that in males.

*Low metastasizing power.* Metastases have only rarely been demonstrated in adjacent lymph nodes. The evidence indicating remote hematogenous metastases is not as yet clearly definitive. Generalized metastases comparable to those commonly observed in the terminal stages of cancer of other organs have not been described.

*Surgical resectability.* Technical difficulties in surgical resection are almost invariably due to the inflammatory complications of prolonged bronchial obstruction rather than to mediastinal invasion or lymph-node involvement.

*Low operative mortality rate.* The operative mortality rate is approximately 10 per cent, depending somewhat on whether a lobectomy or a total pneumonectomy is performed.

*Permanent cures by resection.* Patients surviving resection appear to be permanently cured. No case has been reported in which the patient died of recurrence or metastases.

*Central location.* With rare exceptions, the tumors occur in the large bronchi near the hilum and are thus within easy reach of the bronchoscope.

*Typical histologic pattern.* Small uniformly sized cells are arranged in columns, showing few if any mitoses. Bone formation is not unusual.

If tumors with these characteristics are set aside, it will be found that other bronchogenic tumors portray more typically the picture of carcinoma as established for other organs. Such tumors grow rapidly, varying with the degree of cellular differentiation; the greatest age incidence is from forty to sixty years; the sex incidence is predominantly male (as in cancers of the lip, tongue and stomach); metastases are frequent, again varying with cellular type; surgical resectability, the mortality rate of resection and the permanence of surgical cure are discouraging, favorable results depending on early diagnosis, and recurrence or metastases taking a heavy toll among patients surviving operation; the site of the primary lesion may be peripheral or central, varying in relation to the type of cell; the histologic patterns are those of epidermoid carcinoma, adenocarcinoma or undifferentiated carcinoma, as found in other organs.<sup>2</sup>

Controversy regarding these tumors is concerned with definitions and interpretations rather than with the observational facts listed above. It is not the purpose of this review to defend any thesis relative to the nature of bronchial adenomas, or to criticize any proposed system of nomenclature. One point, however, seems sufficiently obvious: if cases of so-called "adenoma" are mingled with cases of other bronchogenic tumors in a study from which conclusions are drawn regarding prognosis or therapy, this fact should be clearly stated by the author. Compilations of the results of surgical therapy<sup>3</sup> or of x-ray therapy<sup>4</sup> are of doubtful value, or may be positively misleading if this simple rule is not observed.

All articles in this series will be published in book form; the current volume is *Medical Progress: Annual, 1940* (Springfield, Illinois: Charles C. Thomas Company, 1941. \$4.00).

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## WAR INJURIES OF THE CHEST

### Statistics

A recent personal communication relative to chest injuries in the present war stated that the mortality in chest cases received from the evacuation following the Battle of France was only 5 per cent, or equal to only one third the mortality in the South African campaign of 1900, which was the lowest hitherto recorded, and one fifth that in World War I.

It is important to realize just what such figures mean, and the following quotation from a book<sup>5</sup> published in 1877 is so pertinent that further comment is unnecessary.

*Apparent increase in ratios of mortality in certain wounds.*—The following fact serves to illustrate the difference which there may appear to be in the relative fatality of certain wounds under hospital treatment, owing to differences in the distances of the hospitals from the places of fighting. During the Crimean War the percentage of fatality of chest wounds, all kinds of chest wounds being taken together, in the French military hospitals was 30.7 per cent. This ratio of mortality was almost the same as it was in the hospitals of the British army. In the French hospitals during the Italian campaign of 1859, however, the mortality was only 18.9 per cent. The altered rate of mortality shown in the hospital returns of the latter war cannot be said to have been due to any diversity in the nature of the wounds inflicted in the field, nor in that of the treatment adopted in the hospitals; it was obviously attributable to the fact that the field-hospitals in the Crimea were close to the places where the wounds were received, while in the Italian War they were situated for the most part at a considerable distance from them. In the Crimea, the patients were received into the ambulances shortly after their wounds had been inflicted; in Italy, owing to the largeness of the number of wounded resulting from the principal battles, and the consequent difficulties of transport, together with the distance of the hospitals, many of the severer cases did not live long enough to be admitted into hospital for treatment,—they died on the field of action itself. The chest wounds among the "killed in action" in Italy were increased in number; the deaths among those treated in hospital were, in proportion, lessened in number. The absolute mortality from wounds of the chest was probably very similar in both the Italian and Crimean wars.

### Body Armor

Full on his breast the Trojan arrow fell  
But harmless bounded from the plated steel.

Pope: *Translation of the Iliad*.

Body armor is used by police officers and agents of the Federal Bureau of Investigation in certain specialized situations. It furnishes good protection from missiles up to velocities of 1000 feet per second. Many attempts have been made to devise a practical body armor for modern warfare.<sup>6</sup> Obviously, no body armor with a weight that is sup-  
portable can be effective against high-velocity direct axial hits.

There seems to be little doubt that body armor can be used to advantage in specialized situations of modern warfare. The high fatality of chest and abdominal injuries, the frequency of injury from projectiles of low velocity and the transportation of troops by motorized equipment rather than by foot all argue for its use. It seems probable that any appreciable reduction in the mortality rate of chest injuries is apter to be achieved by preventive measures of this type than by more efficient methods of evacuation of the wounded.

### Blast Injuries

Longmore<sup>5</sup> in 1877 referred to injuries resulting from the "disturbance by actual molecular agitation produced by the violent impulse of the air," and to "vibratory disturbance of the internal organs near to the surface on which the impact of the projected gas is directly received." He described a terrific explosion of magazines of gunpowder and munitions of war in the French siege park and the adjoining English siege-train enclosure on November 15, 1855, as follows:

There were large numbers who, though not struck by any solid projectile, nor visibly wounded by the impulsive force of the explosion, were yet more or less seriously contused and injured by it. Some suffered from rupture of superficial blood-vessels of the air-passages and lungs, others from mischief to the organ of hearing. Especially prevalent, however, was shock to the general nervous system, and there could be little doubt, from observation, that this was not merely the result of panic but was largely due to actual physical concussion and contusion.

Blast injury is being discussed as a new entity in the present war, probably because of the frequency of its occurrence as a result of bombing from the air. Sutherland<sup>7</sup> describes the blast wave as a spherical shell of compressed air immediately surrounding the explosion. In the compression part of the wave, pressures up to 200 atmospheres have been observed in bomb explosions. The elasticity of compressed air tends to make it recover its original state, and in this way it tends to overshoot its mark so that although the outside shell is compressed a shell of rarefied air is left behind.

The wave of compressed air travels at an enormous speed (with a 60-pound charge, the velocity at thirty feet from the source has been recorded as 1500 feet per second). The duration of the wave of high pressure at any one point is approximately 0.006 second, and of the following phase of low pressure, 0.03 second, varying with the charge and the distance from the source.<sup>8</sup>

The impact of this wave on the human body causes death without signs of external injury. Sometimes there is a small amount of blood trickling from the nose. Capillary hemorrhage

and even laceration of the alveolar walls may be observed at autopsy. If death does not occur immediately, symptoms may appear as late as two to five days after the injury. Cough, shortness of breath and blood stained sputum result from the hemorrhagic exudate into alveolar and interstitial tissue.

Many reports of blast injuries and experimental studies on the mechanism involved are appearing in current English journals.

## ESOPHAGUS

### *Carcinoma*

The relatively recent advance in the surgical management of carcinoma of the esophagus is pointed out by Adams.<sup>9</sup> Before 1934, only in the celebrated case treated by Torek did the patient survive operation by more than two years. Thirteen other technically successful cases are on record, but the patients died of recurrence or metastases.

Since 1938, successful resections on 34 patients have been compiled by correspondence with twelve American surgeons. Of these, 20 are living, and about 50 per cent of the total of sixty eight operations were successful.

It may be stated without qualification that surgery offers a reasonable chance of arresting carcinoma of the esophagus. Palliative results may be secured when permanent arrest is impossible. The value of this achievement is more apparent if it is realized that carcinoma of the esophagus is fourth in frequency of all malignant tumors occurring in men over twenty years of age. It is surpassed in frequency only by cancer of the stomach, lung and rectum.

The procedure of esophageal resection is far from standardized, and at the moment calls for a combination of techniques derived from gastrointestinal, thoracic and plastic surgery. In general, two quite distinct procedures are available, the choice depending on the level of the carcinoma. Approximately 45 per cent of the tumors are located in the lower third of the esophagus. By a trans pleural approach, the diaphragm is divided, and the cardiac end of the stomach, as well as the esophagus, is mobilized. Resection of the tumor bearing area is followed by elevation of the fundus of the stomach into the pleural cavity and anastomosis with the lower end of the divided esophagus, thus re-establishing the continuity of the digestive tract. This operation is also being successfully employed for carcinomas of the cardiac end of the stomach that previously have been considered inoperable when approached by the abdominal route because of extension up the esophagus, or that, if resectable from below, have required a total gastrectomy.

Carcinoma involving the upper two thirds of the esophagus demands a more complicated and mutilating procedure. No operation has been devised that will permit an internal reconstructive resection. The Torek procedure, with modifications, remains the only feasible one. Following the resection of the tumor bearing area, the upper end of the esophagus is drawn out through a cervical incision and is left as an end esophagostomy. The lower end is inverted into the stomach after resection of the lymph nodes at the cardioesophageal angle. A preliminary Beck-Jianu gastrostomy brought well above the costal margin provides for feeding and may be connected with the cervical stoma by a rubber tube. Patients swallow well chewed food quite satisfactorily through such a temporary artificial esophagus. The permanent goal, however, is the construction of a skin tube joining the cervical esophagostomy and the gastrostomy openings.

The execution of details in this complicated program has varied greatly, and further experience will undoubtedly point the way to simpler methods. At the present time, its successful application calls for versatility and judgment on the part of the surgeon, and patience as well as courage as the contribution of the patient.

### *Congenital Atresia*

A study of 32 cases of congenital atresia of the esophagus has been presented by Lanman.<sup>10</sup> There was a fatal outcome in all the 30 operative cases, but it is evident that considerable progress along rational lines has been made. Lanman recommends a direct anastomosis if possible, otherwise, closure of the tracheoesophageal fistula is advised as the first step. As soon as conditions permit, the subsequent procedures are, first, the exteriorization of the upper esophageal segment and, secondly, an anterior gastrostomy. I have recently had the opportunity of examining a well-developed and well-nourished child at the University of Minnesota Hospital whom Dr Nathaniel L. Leven has brought well into the second year of life by the latter procedure. The problems of the construction of an artificial esophagus in this child are being postponed until a suitable age.

Lanman confesses that he dreads to commit an infant to the sort of existence that this deformity entails, and I must admit that this very consideration has led me to limit my own efforts in dealing with congenital atresia to attempts at direct anastomosis. Needless to say, they have been uniformly unsuccessful, but perhaps technically progressive.

An indirect report has reached me that a successful anastomosis has been achieved at the University of Michigan by Dr Cameron Haight. If

this report is confirmed, the score will be even for the two methods of approach.

Other anomalies of development are frequently associated with atresia of the esophagus and tracheoesophageal fistula. Lanman records in his series 7 cases of associated anomalies, which if not treated by operation were in themselves incompatible with life. In working with such infants, one not infrequently recalls the interpretation of Oliver Wendell Holmes:

Many affections which art has to strive against might be easily shown to be vital to the well-being of society. Hydrocephalus, tabes mesenterica, and other similar maladies are natural agencies which cut off the children of races [that is, strains] that are sinking below the decent minimum which nature has established as the condition of vitality, before they reach the age of reproduction. They are really not so much diseases, as manifestations of congenital incapacity for life; the race would be ruined if art could ever learn always to preserve the individuals subject to them. We must do the best we can for them, but we ought also to know what these "diseases" mean.

### Cardiospasm

The true nature of the disorder of the cardia associated with dilatation of the esophagus has been under discussion for years. Mosher<sup>11</sup> concluded that the fundamental lesion was not spasm but fibrosis of the terminal portion of the esophagus secondary to inflammatory changes starting in adjacent organs. The theory of achalasia of the cardiac sphincter associated with the name of Hurst is well known, but leaves the matter as a "chronic and progressive lesion of Auerbach's plexus," which is still far from satisfying.

An interesting concept has been proposed from Brazil (Etzel<sup>12</sup>), where the disease is said to occur with great frequency, and almost exclusively, among poor country people. Etzel is convinced that not only megaesophagus but megacolon and other associated conditions are the manifestations of a degenerative neuropathy of the intramural part of the autonomic nervous system caused by chronic and incomplete deficiency of vitamin B<sub>1</sub>. Evidence to support this hypothesis is derived from histologic studies and animal experimentation. Citation is made of MacCarrison's work describing enteric lesions in B<sub>1</sub> avitaminosis, in which lesions of a degenerative type were disclosed in Auerbach's plexus.

If this hypothesis can be confirmed, it is necessary to postulate a subclinical avitaminosis producing irreversible degeneration of certain cells of the autonomic system. The known tendency for the onset of the clinical syndrome to be associated with anxiety states or psychic trauma suggests that psychosomatic channels simply provide the trigger mechanism.

The treatment of the disease is usually satisfactorily carried out by dilatation. In complicated or intractable cases, an esophagocardioplasty may be recommended. Even with complete symptomatic relief of the obstructive symptoms, the megaesophagus persists.

### BRONCHIECTASIS

Two important studies throw light on the prognosis of untreated bronchiectasis and indicate that the extension of radical surgery in the treatment of this disease has been justified by the poor outlook under other forms of therapy. Perry and King<sup>13</sup> issued a report based on 260 patients not treated by major operations. Of a group of 211 patients traced, 66 are known to be dead, a mortality rate of 31 per cent. Forty-one per cent of these had died within five years of the onset of symptoms. The series includes recently diagnosed cases, so that the mortality rate reflects only partly the toll that may be assumed in a late follow-up study. Seventy-eight per cent of the deaths were directly attributable to the disease.

Bradshaw et al.<sup>14</sup> report on 171 patients with bronchiectasis, excluding those cases attributable to foreign body or pulmonary abscess, and excluding those patients treated by major surgery or regular bronchoscopic aspirations. In these patients, the diagnosis was established between the years 1925 and 1935. Fifty-nine, or 34.5 per cent, died from bronchiectasis or its complications. The average duration of life in the dead patients from the onset of symptoms was thirteen and a half years.

The conclusion is justified that bronchiectasis is a fatal disease. Death occurs most commonly from pneumonia, and also from pulmonary abscess and gangrene, brain abscess, empyema and, rarely, hemorrhage.

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# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

## CASE 27351\*

### PRESENTATION OF CASE

A 3½ pound newborn infant was admitted four hours after delivery because of prematurity, having been born early in the eighth month of pregnancy, by spontaneous breech delivery after seven hours of labor.

The family history was noncontributory. The mother had been well during pregnancy, and the cause of the premature delivery was not known.

At birth, the baby responded well, had a good cry, and allegedly was not cyanotic. Physical examination on entry revealed a small, fairly well developed, moderately cyanotic infant whose temperature was 95.6°F. The respirations were regular, but there was slight dullness posteriorly, with a few scattered rales at both bases. The heart and abdomen seemed normal.

Examination of the blood showed a red cell count of 5,850,000, and a white cell count of 21,600 with many young cells of both the white and red series. The differential count was 40 per cent polymorphonuclears, 48 per cent lymphocytes, 5 per cent monocytes, 6 per cent eosinophils, and 1 per cent basophils, with normal platelets.

The baby was placed in a high oxygen concentration in a heated cradle, and whenever taken out became cyanotic. Lumbar puncture on the morning after admission revealed grossly bloody fluid. During the second hospital day, respirations became irregular, the color poor, and the cry weak. Respirations ceased that afternoon, twenty-four hours after birth.

### DIFFERENTIAL DIAGNOSIS

DR. THEODORE H. INGALLS: Here we have a baby born prematurely by breech extraction, weighing 3½ pounds at birth, who seemed relatively normal after delivery. Subsequently, he developed increasingly grave spells of cyanosis; dullness and rales appeared at the bases of the lungs. The patient rapidly failed and died within twenty-four hours.

The most striking symptom we have to consider is cyanosis. Cyanosis occurs when the concentration of reduced hemoglobin in the blood reaches

approximately 5 gm per 100 cc. It is well to bear in mind that cyanosis is not necessarily synonymous with anoxia of tissue cells, although of course it may be the precursor. The first possible cause of cyanosis in this case is the interference with continuous respiratory exchange, which to some degree at least is a normal happening at birth. Although some babies are never cyanotic at birth, many are quite blue, and many are absolutely livid before they take their first gasp. In this particular case, however, we are given to believe that neither the attending physician nor, subsequently, the nurses were alarmed about the baby's color.

Secondly, cyanosis can be caused by cardiac and pulmonary disturbances, such as the admixture of venous blood with arterial blood through pathologic openings associated with congenital heart disease. Except for the cyanosis, no other findings in this case draw one's attention particularly to the heart. Atelectasis may be a cause of cyanosis. However, simple atelectasis as the only cause of the failure of the lungs to expand is not a satisfactory diagnosis in my opinion. Gross abnormalities of the bronchial tree or the inspiration of such large amounts of mucus and amniotic fluid that the baby practically drowns would result in atelectasis, but one would expect the appearance of the symptoms soon after birth.

This brings me to the final and most serious cause of cyanosis—cerebral injury, which may result from asphyxia, trauma, hemorrhage, edema or a combination of these. In fact, they are usually combined. Following asphyxia, for example, the first result is congestion, then edema, then necrosis and finally hemorrhage. In this case, a very tangible suggestion that there was cerebral injury is grossly bloody lumbar puncture. Such a finding is also consistent with the fact that this baby was distinctly premature. The fragile underdeveloped tissues of the premature infant make him particularly susceptible to cerebral injury, so that he is frequently unable to withstand even the normal stress and strain and anoxemia of delivery. In this case, birth was by breech extraction, which is a distinct central-nervous system hazard.

The symptoms of cerebral hemorrhage depend on the size, the site and the propagation of the hemorrhage. If there is slowly accumulating subarachnoid bleeding, there may be irritation of the cortex, and convulsions may ensue. If there is subtentorial bleeding, cyanosis may be the predominant symptom. In this case, a suggestion that this may have occurred is the fact that the baby's fontanelle is not mentioned as bulging. Finally, we have the findings in the chest to in-

\*This case is published through the courtesy of the Children's Hospital.

terpret—dullness and rales at the bases of the lungs, which I should think represented pulmonary edema due to injury of the vagal nuclei; if both vagi are injured in the experimental animal, pulmonary edema follows consistently in the space of twelve to twenty-four hours. It is not possible to rule out pneumonia, although I am under the impression that pulmonary edema is more often misdiagnosed as terminal pneumonia than the reverse. I shall be interested in the pathological report on the lungs, however.

Finally, I think I should merely mention vitamin K deficiency in passing as being a possible, or at least a contributory, cause of bleeding, although in this case the only clinical suggestion of bleeding is the bloody lumbar puncture.

DR. ELI C. ROMBERG: It would have been interesting to know whether the baby had any slowing of the pulse and of respirations, because all the premature infants who have those symptoms and intermittent cyanosis, and die within thirty-six hours, have subtentorial hemorrhage.

DR. HAROLD L. HIGGINS: The striking thing about this case to me is that we are dealing with a premature infant, and I cannot help believing that a most likely cause of death was the inability of the child's brain to maintain normal respiration and circulation, because of immaturity. I realize that an intracranial hemorrhage was suspected, because a lumbar puncture was done; but I wonder if there was bulging of the fontanelle or other signs of increased pressure. Again, was the blood found on spinal puncture due to trauma? I should certainly suspect vitamin K deficiency as a contributing cause of the hemorrhage. My diagnosis would be prematurity, with probable cerebral hemorrhage, hemorrhagic disease of the newborn and traumatic injury at birth.

#### CLINICAL DIAGNOSES

Prematurity.  
Cerebral hemorrhage.

#### DR. INGALLS'S DIAGNOSES

Prematurity.  
Cerebral hemorrhage (? subtentorial).  
Pulmonary edema (? pneumonia).

#### ANATOMICAL DIAGNOSES

Pneumonia (pneumococcus).  
Pneumococcemia.  
Pulmonary edema and congestion.  
Aspiration of amniotic-sac contents.  
Cerebral hemorrhage, subarachnoid and subdural.  
Prematurity.

#### PATHOLOGICAL DISCUSSION

DR. SIDNEY FARBER\*: I think the fact that so many possibilities have been mentioned in the thorough review that Dr. Ingalls gave, in addition to the fact that different suggestions have been made concerning what the infant might have had, is characteristic of the problem of the premature infant. This infant weighed  $3\frac{1}{2}$  pounds, and died twenty-four hours after entering the hospital. At autopsy, there was diffuse hemorrhage beneath the arachnoid and beneath the dura, and a hematoma of the scalp. So much for the cerebral difficulty. There was a very early pneumococcal pneumonia. The pneumococcus was grown from the heart's blood and the lung. Furthermore, in the lungs, there was evidence of aspiration of amniotic-sac contents and considerable congestion and edema. Fibrin thrombi were found microscopically in many organs of the body, a finding that may be explained by the pneumococcemia.

I should like to say before going farther that prematurity or immaturity of tissues alone is in my opinion an unsatisfactory cause of death or of any important disturbance in a baby weighing  $3\frac{1}{2}$  pounds. Although immaturity of the tissues is usually demonstrable, particularly in the brain, I believe that a baby of this weight has achieved enough maturity of development to get along perfectly well and to live without having serious symptoms referable to immaturity of tissues.

The meninges were extremely thin. The superficial vessels were congested, and there was diffuse subarachnoid hemorrhage scattered over the various brain surfaces. Some of this appeared to be quite recent and it is probable that not all the hemorrhage took place during labor. There was no collection of blood over the cerebellum or brain stem, sites of involvement that would cause much more intense cyanosis or much more difficulty with respiration than the type of hemorrhage encountered here. If we find no more cerebral hemorrhage than we found here, we must look elsewhere for a satisfactory explanation of the cyanosis. A premature baby rarely suffers from tentorial tears or rupture of the great veins of Galen. Gross tears of the dural membranes do not occur so frequently as in full-term babies.

The mode of entrance of the pneumococci was by way of the aspirated amniotic contents, which had been infected with the organisms from the birth canal of the mother.

In summary, there was diffuse cerebral hemorrhage as a part of a general birth injury. This

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was a contributory cause of death and of the cyanosis. The immediate cause of death was the pneumococemia, which spread to the blood stream from the lungs. The pneumococcus apparently entered the lungs with aspirated amniotic-sac contents, which were infected from the birth canal of the mother.

DR. HIGGINS: One wonders about infection as the result of mouth-to-mouth insufflation.

DR. FARBER: That would be quite possible as the means of entrance of the organisms.

A PHYSICIAN: Is the white-cell count of 22,000 high?

DR. INGALLS: I should consider it moderately high for a premature infant; it did not strike me as pathognomonic of infection.

DR. HIGGINS: Do you not think, Dr. Farber, that one can get functional immaturity without pathological immaturity?

DR. FARBER: I am quite sure one could. My point, Dr. Higgins, is that, although immaturity of the respiratory center is of importance and is one of the factors that combined with others may bring about atelectasis and respiratory difficulty, immaturity alone is not explanation enough for respiratory disturbance in a premature baby.

## CASE 27352

### PRESENTATION OF CASE

*First Admission.* A forty-three-year-old American roofer entered the hospital complaining of a skin rash.

Three years before entry, he noticed a slightly raised reddish itching patch about 1 cm. in diameter on the inside of the right thigh. Since then, similar lesions had appeared all over his body, including the abdomen, back, chest and the flexor surfaces of the lower legs and arms. No lesions had ever appeared on the extensor surfaces of the arms or legs or on the head. The lesions were usually round at the onset and finally became completely irregular. Some of them developed brown crusts; others became rough, without crusts. The lesions usually lasted about three weeks and left no marks. There was no seasonal distribution. Three months before entry, a crusting lesion appeared in the right groin. This swelled considerably and then disappeared.

The family, marital and past histories were non-contributory.

Physical examination showed a well-developed and well-nourished man lying in bed without discomfort. Over the back of the neck, the flexor surfaces of the arms, and over the back and abdo-

men, there were slightly raised pink lesions varying from 1 to 4 cm. in diameter. Some were irregularly bordered, others sharply outlined. Many showed only slight scaling, whereas others had a grayish crust.

The temperature was 98.4°F., the pulse 80, and the respirations 20.

Examination of the urine was negative. The blood showed a red-cell count of 5,090,000 with a hemoglobin of 75 per cent, and a white-cell count of 5650 with 74 per cent polymorphonuclears.

An x-ray film of the chest showed that the right lung field was slightly less radiant than the left, and that the intercostal spaces were narrowed. There was evidence of thickening of the pleura from the apex to the diaphragm, but no definite areas of consolidation within either lung. The lung roots were slightly thickened. There were no mediastinal masses.

On the fifth day, a biopsy of one of the skin lesions was taken, and an axillary lymph node removed. The skin showed the histologic structure of mycosis fungoides, but the axillary lymph node showed only chronic inflammation. The patient was discharged on the following day, after having received x-ray treatment and one intravenous injection of arsphenamine.

*Final Admission* (approximately four years later). Following discharge, he was seen fairly often, receiving on the average one x-ray treatment a month. The larger lesions were fairly well controlled by this treatment. Seven months before entry, while in Maine, he developed a very large lesion on the right thigh. He went to another physician, who gave him three doses of very deep x-ray therapy, the last one about a month before entry. This treatment, according to the patient, "knocked the stuffing out of him," and he was forced to go to bed. He was very weak and had a very poor appetite. During the month before this admission, he developed slight shortness of breath, and about a week later, an abscess in the left axilla, which discharged spontaneously.

Physical examination showed an emaciated, anemic, cachectic man, with generalized, blotchy, red and pigmented, scaly, macular areas, and also several infiltrated plaques and nodules over the skin. There was generalized lymphadenopathy. The mucous membranes were pale but showed no lesions. There was slight bronchovesicular breathing over both bases, but no rales. The heart sounds were of poor quality. The blood pressure was 100 systolic, 55 diastolic. The liver edge was felt 5 cm. below the costal margin. The spleen was felt 5 cm. below the umbilicus and in the flank.

The temperature was 102°F., the pulse 110, and the respirations 20.

Examination of the urine was negative. The blood showed a red-cell count of 3,190,000 with a hemoglobin of 65 per cent, and a white-cell count of 5400 with 64 per cent polymorphonuclears. The platelets were markedly decreased. The red blood cells showed mild achromia. A blood Hinton reaction was negative. The bleeding time was 3 minutes.

An x-ray film of the chest was negative.

The patient was given fluid parenterally. The temperature remained fairly elevated, ranging between 100 and 102°F. The red-cell count dropped to 1,160,000, with a hemoglobin of 35 to 40 per cent. The white-cell count dropped to 2600 and finally to 1250. A smear showed marked achromia and variations in size and shape of the red blood cells. No platelets or young forms were seen. There was approximately 70 per cent polymorphonuclears. The patient failed rapidly, and died sixteen days after admission.

#### DIFFERENTIAL DIAGNOSIS

**DR. WALTER F. LEVER:** A differential diagnostic discussion of the cutaneous lesions is superfluous, because the diagnosis "mycosis fungoides" had already been established by histologic examination, four years before the patient's death. In addition to the cutaneous eruption, the patient presented a generalized lymphadenopathy, a marked increase in the size of the liver and spleen, and a severe anemia, leukopenia and thrombocytopenia. The question arises whether any or all these manifestations were caused by mycosis fungoides.

According to the present prevailing view, mycosis fungoides is a form of lymphoblastoma. Under lymphoblastoma are grouped all neoplasms derived from the stem cell, which is the mother cell of both the lymphatic and the reticulum cells. The infiltrate of mycosis fungoides contains, in varying proportions, stem cells and both types of cells derived from the stem cell, so that histologic examination may show stem cells, lymphoblasts, lymphocytes, reticulum cells and monocytes. In addition to these, a variety of other cells are usually present in the infiltrate, namely granulocytes (neutrophils, as well as eosinophils) fibroblasts, fibrocytes and plasma cells, all of which are mature. The latter group of cells represents merely an inflammatory reaction provoked by the neoplastic infiltrate. This inflammatory reaction is most pronounced in the early stages of the disease, so that histologic examination at that time may show only mature cells, as found in chronic inflammation. If the neoplastic process involves

mainly the lymphatic cells, mycosis fungoides may, histologically as well as clinically, resemble lymphocytic lymphoblastoma; if the infiltrate is made up mainly of reticulum cells, the histologic picture of mycosis fungoides may resemble reticulum-cell lymphoblastoma; if both types of cells are present in a more or less equal proportion, mycosis fungoides may histologically resemble Hodgkin's disease. There even exists strong evidence that mycosis fungoides is actually identical with any of the three above-mentioned types of lymphoblastoma, and that it differs from them only clinically in its tendency to primary and preponderant localization in the skin.

The classification of mycosis fungoides into the group of lymphoblastomas and the realization of its close relation to, if not identity with, lymphocytic lymphoblastoma, reticulum-cell lymphoblastoma and Hodgkin's disease explain the occasionally encountered widespread neoplastic involvement of internal organs in mycosis fungoides.

Applying this concept to the present case, I believe that histologic examination of some lymph nodes showed neoplastic changes involving either the lymphatic or the reticulum cells, or both types of cells simultaneously, whereas other lymph nodes showed only an inflammatory infiltration, just as the cutaneous lesions of mycosis fungoides may present either a neoplastic or merely an inflammatory infiltrate.

The considerable enlargement of the liver and spleen was, in my opinion, also due to an infiltration with neoplastic lymphoblastic cells. Other causes than lymphoblastoma can be ruled out fairly well. The tremendous size of the spleen readily rules out the possibility of cirrhosis of the liver, or of cardiac decompensation or amyloidosis. Furthermore, there were no collateral symptoms to substantiate these diagnoses.

There are three possible explanations of the aplastic anemia. First, the aplastic anemia may have been due to lymphoblastic involvement of the bone marrow (myelophthisis). Secondly, it may have been merely a terminal, nonspecific, toxic process caused by cachexia, and thirdly, it may have been the result of the extensive x-ray therapy. In mycosis fungoides, bone-marrow changes are fairly frequent but, as a rule, are present only in a mild degree. They occur mainly in the form of an increase in the number of stem cells and their immature derivative cells. These bone-marrow changes of mycosis fungoides may occur with or without changes in the number and appearance of the circulating blood cells. Yet, one should think that an unusually severe involvement, which in the end completely prevented the



mission of red and white blood cells into circulation, would have led to an appearance of immature blood cells during the preceding weeks. In view of the absence of qualitative changes in the peripheral blood, I am inclined to believe that the aplastic anemia was a nonspecific toxic terminal process. The extensive x-ray radiation may have been a contributory factor. I believe it will be impossible to determine how much either factor was responsible. In any case, I should expect the bone marrow to show the usual appearance in aplastic anemia (fatty, gelatinous degeneration, and microscopically almost complete absence of red cells, myelocytes and megakaryocytes).

In conclusion, I want to point out the clinical resemblance of this case of mycosis fungoides to one of Hodgkin's disease. I believe that the resemblance to Hodgkin's disease will be borne out by the histologic examination.

#### CLINICAL DIAGNOSIS

Mycosis fungoides

#### DR. LEVER'S DIAGNOSES

Lymphoblastoma (mycosis fungoides, ? Hodgkin's disease) of the skin, lymph nodes, liver and spleen

Aplastic anemia (terminal toxic, with x-ray irradiation possibly a contributory factor)

#### ANATOMICAL DIAGNOSES

Mycosis fungoides

Aplastic anemia

Pulmonary infarction, septic, multiple, bilateral

Infarct of spleen

Operative wound biopsy, left epitrochlear gland

Arteriosclerosis, slight, aortic

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY. Dr. Lever's predictions proved very close to what we actually found at autopsy. The primary diagnosis had, of course, already been established histologically by the biopsy. There is, however, great variety among these cases in the type of infiltrating cells and in the degree of involvement of the internal organs. In this case, there was obvious lymphomatous involvement of a large proportion of the

lymph nodes of the body and also of the spleen. The liver, however, did not contain neoplasm and showed only a mixture of fatty infiltration and central necrosis of the lobules. It was not strikingly large, weighing 1800 gm., whereas the spleen, which weighed 1100 gm., is well up to the size seen in leukemia. Dr. Lever was correct in stating that the bone marrow would not be replaced by tumor cells but would be consistent with aplastic anemia. It showed a great diminution in the hematopoietic elements of both the red cell and white-cell series, a slight increase in the number of fat cells and a considerable degree of so-called "gelatinous degeneration." There were no other significant findings.

From the point of view of histologic classification, the neoplastic cells all showed differentiation in the direction of relatively mature lymphocytes. It would have been impossible, for instance, to distinguish sections of the spleen and lymph nodes from those of corresponding tissues from a case of lymphoid leukemia. As Dr. Lever has pointed out, this is by no means always so. Even when there is a marked generalized lymphadenopathy, one is often disappointed that a lymph node removed for biopsy shows only a nonspecific hyperplasia and nothing on which a diagnosis of lymphoma can be made. The diagnosis of the disease must usually be made from a biopsy of the skin itself. In the early stages, this is often extremely difficult, and sometimes several biopsies must be taken before the diagnosis can be established. The period of time during which the process may remain localized to the skin is often, in comparison with other lymphomatous processes, astoundingly long. Five and ten years are not uncommon figures, and intervals as long as fifteen years are sometimes observed.

I can go no farther than Dr. Lever did in explaining the cause of the aplastic anemia. It may have been some effect of the neoplastic process, or of the chronic sepsis that so often supervenes in the terminal stages of this disease when the skin tumors break down and ulcerate. Prolonged x-ray exposure can certainly produce this type of bone marrow, and in the course of years these patients often receive a formidable amount of radiation.

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This bill provides that no couple may receive a marriage license until they can provide the town or city clerk who issues it certificates showing that a registered practitioner of medicine has examined each party and has explained his findings to both

parties. A blood test for syphilis is to be part of the examination. A law with similar provisions has been in successful operation in Virginia for nearly two years.

The wording of the bill makes it mandatory for the physician to find or exclude any "infectious disease declared by the State Department of Public Health to be dangerous to the public health." This means that all so-called "reportable diseases" must be considered. The bill in no way changes present laws in connection with the reporting to local boards of health of cases found to have any of these infections.

The law makes no provision for halting any marriage; but if its provisions are carried out conscientiously by the profession, men and women will be prevented from marrying obviously sick persons without being so informed in advance. Furthermore, if disease is found, an opportunity is provided for the treatment of the infected prospective partner and for the protection of the other after marriage.

The bill puts a very great responsibility on those members of the profession who will make these examinations, but the duty should not be shirked and overcharges should be avoided. Nominal charges for very careful examinations might well result in creating friendships that would lead to many calls for obstetric or other medical service in later years. Furthermore, such an approach would be peculiarly effective at the time when nearly all couples, no matter how wealthy they may be, feel poor because of the large expenses necessarily incurred in setting up a home.

Nearly all premarital laws in other states focus their emphasis on "blood testing" and also attempt to prevent marriage under certain conditions. The difficulty with such provisions lies in the impracticability of setting up fair and workable laws that will cover all the various contingencies. This difficulty is recognized in some states, such as New York, by providing that certain judges have the power to authorize marriages otherwise forbidden when "public policy" makes such a step seem proper. A difficulty with this is that judges as a class are not trained in medicine or public health

id must act on information secured from physicians. It seems much better to leave the whole matter to physicians, and to remove all possible impulses beyond the determination and presentation of medically determined facts

## PROCUREMENT AND ASSIGNMENT AGENCY

ALTHOUGH over 160,000 physicians have filled out the questionnaires forwarded by the Committee on Medical Preparedness of the American Medical Association, and although these invaluable data concerning professional training, experience and availability have been transferred to punch cards at the headquarters of the association, as yet no authority has been created with the power to make use of this material

As pointed out in *War Medicine*,\* the future needs for medical personnel will probably include the following physicians for the United States Army, Navy and Public Health Service and other governmental agencies, physicians for the local and appeal boards created under the Selective Service Act, physicians for civilian medical care and defense, physicians for aid to Britain, requested by the American Red Cross, physicians for industry, physicians for rehabilitation, and physicians for state and county medical and public health organizations. The procurement and assignment of men to fill these positions to best advantage is a tremendous task, but one that could be properly handled if the punch card data were utilized. For this reason, the House of Delegates, at the recent meeting of the American Medical Association, passed a resolution urging the establishment, by the United States government, of a central authority, to be known as the Procurement and Assignment Agency, to provide, if necessary, for efficient and adequate medical staffing of all governmental, civilian and industrial services. The membership of such an agency would include representatives of the civilian medical profession

Copies of this resolution were forwarded to the

various governmental heads in Washington who are concerned with the problems of medical care, and it is hoped that prompt action will be taken and that means will thus be created for the provision of a wisely selected medical personnel in any emergency

## MEDICAL EPONYM

### BENCE JONES PROTEIN

A paper, "On a new substance occurring in the Urine of a patient with Mollines Ossium," was read before the Royal Society on April 22, 1847, by Henry Bence Jones (1813-1873), physician to St George's Hospital. This appears in the *Philosophical Transactions of the Royal Society of London* (138, Pt 1 55-62, 1848)

On the 1st of November 1845 I received from Dr *Watson* the following note with a test tube containing a thick, yellow, semi-solid substance — The tube contains urine of very high specific gravity when boiled it becomes highly opaque, on the addition of nitric acid it effervesces assumes a reddish hue, becomes quite clear, but, as it cools assumes the consistency and appearance which you see heat relieves it. What is it?

A few hours afterward a specimen of the same urine, passed by a grocer forty seven years of age, who had been out of health for thirteen months was sent to me by Dr *MacIntyre*. He, being in attendance on the case with Dr *Watson*, had two days previously first observed the peculiar reactions of the urine.

The specimen of urine was slightly acid, specific gravity 1034, it contained a sediment consisting of crystalline phosphate of lime, oxalate of lime, and cylinders of fibrin. The urine became thick with heat from a deposit of phosphates, but cleared with a drop of acid. It gave no precipitate with an excess of nitric acid, unless left to stand, or unless heated and left to cool, when it became solid. This solid redissolved by heat, and again formed on cooling. Continued boiling with strong nitric acid evolved but little gas, and did not quickly hinder this reaction. Hydrochloric acid gave the same solid precipitate, soluble by heat. Strong acetic acid gave only a slight precipitate which redissolved by heat. Caustic potash and sulphate of copper gave a splendid bright blue, clear liquid, passing over when heated to claret colour.

January 2nd — The patient died. The following day I saw that the bony structure of the ribs was cut with the greatest ease, and that the bodies of the vertebrae were capable of being sliced off with the knife. For an account of the structure of the bone, see a paper by Mr *Dalrymple* in the third number of the *Dublin Journal*, August 1846.

The ultimate analysis of this substance may be represented by  $C_{48} H_{37} N_6 O_{15}$  or  $C_{40} H_{30} N_5 O_{12}$

Hence it is an oxide of albumen, and from ultimate analysis, it is the hydrated deuteroxide of albumen

\*Editorial A procurement and assignment agency *War Med* 1 536-538

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parties. A blood test for syphilis is to be part of the examination. A law with similar provisions has been in successful operation in Virginia for nearly two years.

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ons should be established Ether and iodine have been proved bactericidally to be as good as any other preparations and better than most, and the iodine solution costs less than 10 cents a pint, a figure much lower than those of other antiseptic solutions

This patient evidently was septic from the beginning, and it is quite likely that she was suffering from a pelvic phlebitis. The use of uroquinolone during the convalescence suggests that pyelitis was wrongly diagnosed. There is no excuse for allowing a patient who has had tenderness in the leg and an elevated temperature on and off for eighteen days to get out of bed. This sepsis, which was undoubtedly caused by an embolus, and which might have been prevented by conservative treatment, was due to poor medical care.

## COMMITTEE ON STATE AND NATIONAL LEGISLATION

The following is a transcript of House Bill No. 60, recently signed by Governor Saltonstall

**AN ACT** further regulating the filing of notices of intention of marriage, and the delivery of certificates of such intention and the return of unused certificates

Section 1 Chapter two hundred and seven of the General Laws is hereby amended by inserting after section twenty A, inserted by section three of chapter two hundred and sixty nine of the acts of nineteen hundred and thirty nine, the following new section

Section 20B Except as hereinafter provided, such notice of intention of marriage shall not be accepted by the clerk or registrar until he has received from each party to the intended marriage a certificate signed by a registered physician who has examined such party as hereinafter provided. If such physician, in making such examination, discovers evidence of any infectious disease declared by the state department of public health to be dangerous to the public health, he shall inform both parties of the nature of such infectious disease and of the possibilities of transmitting the same to his or her marital partner or to their children. Such examination shall include a standard serological test for syphilis and said test shall be made by a laboratory of said department or by a laboratory approved by it for such test.

Such certificate shall read as follows—I (name and address of physician), a registered physician of (city or town) in the commonwealth of Massachusetts on oath declare that on (day, month, year) I examined (name and address of party) in accordance with section twenty B of chapter two hundred and seven of the General Laws

The examination by such physician and the laboratory test shall be made not more than thirty days before the filing of the notice of marriage. Whoever fails to comply with this section shall be punished by a fine of not less than ten nor more than one hundred

dollars. In extraordinary or emergency cases where the death of either party is imminent or where the female is near the termination of her pregnancy, upon the authoritative request of a minister, clergyman, priest, rabbi or attending physician, the clerk or registrar may accept such notice of intention without having received the physician's certificate hereinbefore referred to

Section 2 Section twenty eight of said chapter two hundred and seven, as appearing in the Tercenary Edition, is hereby amended by striking out, in the third and in the eleventh lines, the words 'six months' and inserting in place thereof, in each instance, the words, 'sixty days,' so as to read as follows—

Section 28 On or after the fifth day from the filing of notice of intention of marriage, except as otherwise provided, but not in any event later than sixty days after such filing, the clerk or registrar shall deliver to the parties a certificate signed by him, specifying the date when notice was filed with him and all facts relative to the marriage which are required by law to be ascertained and recorded, except those relative to the person by whom the marriage is to be solemnized. Such certificate shall be delivered to the minister or magistrate before whom the marriage is to be contracted, before he proceeds to solemnize the same. If such certificate is not sooner used, it shall be returned to the office issuing it within sixty days after the date when notice of intention of marriage was filed.

Section 3 Section fifty seven of said chapter two hundred and seven, as so appearing, is hereby amended by striking out, in the second and in the fourth and fifth lines, the words 'six months' and inserting in place thereof, in each instance, the words, 'sixty days,' so as to read as follows—

Section 57 Whoever performs a ceremony of marriage upon a certificate more than sixty days after the filing of the notice of intention of marriage as set forth in such certificate, and whoever having taken out such certificate and not having used it fails to return it, within sixty days after such filing, to the office issuing the same, shall be punished by a fine of not more than ten dollars.

Section 4 This act shall not affect any certificate referred to in section twenty-eight of chapter two hundred and seven of the General Laws which was lawfully issued and outstanding upon the effective date of this act.

HENRY C. MARBLE, *Chairman*

## DEATH

**TRACY**—WILLIAM L. TRACY, M.D., of Pittsfield, died recently. He was in his sixty seventh year.

Born in Hartland, New Brunswick, he attended Fredrickton Normal School and the University of New Brunswick, and received his degree from McGill University Faculty of Medicine in 1908. He was treasurer and chief surgeon of Hillcrest Hospital, Pittsfield.

Dr. Tracy was a fellow of the Massachusetts Medical Society, the American Medical Association and the American College of Surgeons. He was president of the Pittsfield Surgeons Club and was treasurer of the Pittsfield Cancer Clinic.

His sister, two nieces and five nephews survive him.

## MISCELLANY

## AMERICAN MEDICAL DIRECTORY

About September 1, an information card will be sent from the headquarters office of the American Medical Association to every physician in the United States and Canada. The information secured is to be used in compiling the seventeenth edition of the *American Medical Directory*.

The directory is prepared at regular intervals in the Biographical Department of the American Medical Association. The last previous edition appeared in 1940. This volume is one of the most important contributions of the American Medical Association to the work of the medical profession in the United States; it has been especially valuable in the medical preparedness program. In it, as in no other published directory, are dependable data concerning physicians, hospitals, medical organizations and activities. The directory provides full information concerning medical colleges, specialization in the field of medical practice, memberships in special medical societies, tabulations of medical journals and medical libraries and, indeed, practically every important fact concerning the medical profession in which anyone might possibly be interested.

Before filling out the information card, physicians should read the instructions carefully. They are especially urged to state whether or not they are on extended active duty for the medical reserve corps of the United States Army and Navy. The card should be filled out and returned promptly whether or not a change has occurred in any points on which information is requested. If a change of address occurs before March 1, 1942, it should be reported at once. If any physician fails to receive a card before October 1, he should write at once to the headquarters office stating that fact, and a duplicate card will be mailed.

## NOTES

Three National Scholarships, the outstanding awards to students entering Harvard Medical School this fall, were recently announced by Harvard University. The recipients are Gaston E. Blom, of Tuckahoe, New York, A.B. Colgate University '41; William F. Ketchum, of Evanston, Illinois, A.B. Harvard '41; and Frederick R. Gilmore, of Bloomsburg, Pennsylvania, A.B. Lehigh University '41. This is the fifth year of the medical school's National Scholarship plan, which is similar to that introduced in Harvard College in 1934, and subsequently adopted by the Graduate School of Arts and Sciences, the Graduate School of Design and the Graduate School of Business Administration.

In addition, medical-school scholarships and fellowships totaling \$6,860, for study during the next academic year, were awarded as follows: Matthew and Mary E. Bartlett Scholarship to Harold D. Rosenbaum, of Fair Play, Kentucky; James Jackson Cabot Fellowship to Carl T. Nelson, of Jamaica Plain, Massachusetts; DeLamar student research fellowships to William E. Watts, of Seattle, Washington, Victor C. Vaughan, 3rd, of Richmond, Virginia, and Israel H. Scheinberg, of New York City; Jeffrey Richardson Fellowship to Eugene R. Sullivan, assistant in medicine, Massachusetts General Hospital; George Cheyne Shattuck Memorial Fellowship to Walter E. Knox, of McCook, Nebraska; Charles Eliot Ware Memorial Fellowship to William F. Pollock, of Santa Monica, California; John Ware Memorial Fellowship to Herbert R. Morgan, of Bell, California; Abraham

A. Watson Scholarship to Stuart G. Quan, of Oakland, California; Whitman Fellowship to Henry S. Fuller, of Washington, D. C.; and Dr. William Hunter Workman Scholarship to Ping-Yang Liu, research fellow in bacteriology and immunology, Harvard Medical School.

The Board of Directors of Oglethorpe University has recently announced the opening of a school of medicine, to be located on the university campus, in the suburbs of Atlanta, Georgia. Clinical facilities will be available at the Lawson General Hospital, Grady Hospital and U. S. Veterans' Hospital No. 48. Dr. John L. Jacobs, formerly professor of bacteriology and immunology at Tufts College Medical School, has been elected vice-president of the university in charge of the scientific work of the institution and is now engaged in the organization of courses, admission of students and preparation of classes. Although the school is primarily intended for Georgia residents, anyone may apply for admission.

At the annual meeting of the Massachusetts Board of Registration in Medicine held July 11, 1941, Dr. Francis R. Mahony, of Lowell, was re-elected chairman of the Board and Dr. Stephen Rushmore, of Boston, was re-elected secretary for the ensuing year.

## BOOK REVIEWS

*Criminal Youth and the Borstal System.* By William Healy, M.D., and Benedict S. Alper. 8°, cloth, 251 pp. New York: Commonwealth Fund, 1941. \$1.50.

Since four out of five of the "graduates" of reformatories for delinquents and young criminals commit further offenses on their release, any investigation made by competent scholars on the methods of preventing this human waste ought to be welcomed not only by sociologists and criminologists but by physicians, whose fine tradition in the healing art, tested by time, might well be projected, both civically and professionally, to co-operate in the prevention of crime.

Criminal careers are mainly a problem of youth, and there has been a startling increase of criminality in the 'teen ages. More major crimes are committed at the ages of nineteen and twenty than at any other age. Previous studies have shown reformatories to be dehumanized, depersonalized and regimented—in other words, inefficient. Although improvement in these institutions is not the sole or even the chief means of prevention, anything to improve their administration would help. Accordingly, the Criminal Justice-Youth Committee of the American Law Institute commissioned Dr. Healy, a noted authority on delinquents, and Mr. Alper to make a study of the Borstal system in Great Britain, which, according to the report presented, seems to work quite well.

The authors sketch vividly the organization, personnel and day-to-day life in Borstal and similar institutions, and they give the reader an intimate account of the whole procedure from court commitment to aftercare and parole. The Commonwealth Fund is to be congratulated on the publication of this able, objective and penetrating report.

*Proctology and the General Practitioner.* By Frederick C. Smith, M.D., M.Sc. (med.). 8°, cloth, 466 pp., with 161 illustrations and 5 color plates. Philadelphia: F. A. Davis Company, 1941. \$4.50.

This book, as the name implies, is primarily written for the general practitioner, but it can also be read with benefit by the general surgeon and the proctologist. It

may be divided into three sections diseases of the anus and the anorectal junction, major diseases of the rectum and colon, and parasitic diseases of the entire gastrointestinal tract.

The greater part of the book is devoted to the first section. The chapters on anatomy, anorectal symptoms, history taking, methods of examination, preoperative and postoperative care, choice and methods of anesthesia, and the treatment of hemorrhoids, fistulas, fissures, acute infection and pruritus are comprehensive. Little known to the proctologist is omitted, although some proctologists will not agree with some of the author's conceptions. The most practical features of all these diseases are clearly presented, omitting all unnecessary details and controversial theoretical considerations.

The chapters on major diseases of the rectum and colon, such as cancer, diverticulitis and ulcerative colitis, are very sketchy, being mere outlines.

The chapter on parasitic diseases of the gastrointestinal tract is long and inclusive. It contains very valuable practical information on clinical parasitology, an outstanding feature of the whole book.

The book is written in simple style, the type is large, and the illustrations are adequate. There are numerous witty expressions and rhetorical phrases to distract the reader from the technical monotony. For example, the author refers to cancer of the rectum and sigmoid as 'the wild beast of the jungle, stalking silently on its victim and giving little warning of its approach until it makes its fatal strike'.

The book makes a valuable addition to the library of the general practitioner.

*The Mask of Sanity: An attempt to reinterpret the so-called psychopathic personality* By Hervey Cleckley, B.S., B.A. (Oxon), M.D. 8", cloth, 298 pp. St. Louis: The C. V. Mosby Company, 1941. \$3.00.

This work is, on the whole, as journalistic as the title. Fourteen cases of psychopathic personality are cited, all of them in men, although there are actually as many women who are psychopathic inferiors as there are men. The case histories are given with great fervor and gusto, intermingled with bits of poetry. In fact, the introduction to the book is apparently an original poem, which begins

From chaos shaped, the Bios grows In bone  
And viscus broods the Id And who can say  
Whence Eros comes? Or chart his troubled way?

The reviewer wonders what this has to do with the psychopathic personality.

The vivid description of the cases is followed by an analysis of the literature, together with the introduction of a new name for the psychopathic inferior, 'semicoma dementia', which means a dementia in the understanding of the meaning of life. If that is the disease from which the psychopathic inferior suffers, this term can be applied to most of us, and certainly to the reviewer, since so far as he knows, no one as yet has given us a real insight into the meaning of life. Psychiatry does not need any new names for old subjects, and progress is not recorded in this way.

No essentially new facts are presented. The book is not literary and fictional enough for a novel, yet it has a little too much literariness for a scientific publication. Its merits reside in the earnest interest of the author and

his emphasis on the seriousness of the problem, although he has no real remedy to offer. In point of fact, no one else has.

*Macleod's Physiology in Modern Medicine* Edited by Philip Bard, Ph.D. With the collaboration of Henry C. Bazett, M.D., L.R.C.P., George R. Cowgill, Ph.D., Howard J. Curtis, A.M., Ph.D., Harry Eagle, M.D., Chalmers L. Gemmill, M.D., Magnus I. Gregersen, Ph.D., Roy G. Hoskins, Ph.D., M.D., J. M. D. Olmsted, Ph.D., and Carl F. Schmidt, M.D. Ninth edition. 8", cloth, 1256 pp., with 124 tables and 387 illustrations. St. Louis: The C. V. Mosby Company, 1941. \$10.00.

The tradition of seven editions of this work under the late J. J. R. Macleod, eminent Canadian physiologist, now edited for the second time by Philip Bard, professor of physiology at Johns Hopkins University, makes it the outstanding treatise in this field. It is not intended to be a textbook in applied physiology, as the title implies. Although the original purpose of the book was to serve as a guide to the clinical application of physiology, the present editor and his collaborators, still devoting a great deal of attention to clinical material, deal with it only so far as it illustrates fundamental principles. They assume that the greatest service which physiology can render modern medicine is to continue to solve fundamental problems, even though they may yet not be of immediate practical application.

One may turn to this volume, then, not only as a rich authoritative source book, but as a pathfinder and pace inaker in modern medicine.

*Handbook of Anaesthetics* (Formerly by Ross and Fairlie). Revised by R. J. Minnitt, M.D. (Liverpool), D.A. (D.C.P. & S. Eng.). With chapters on local and spinal anaesthesia by W. Quarry Wood, M.D., Ch.M., F.R.C.S.E. Fifth edition. 12", cloth, 364 pp., with 103 illustrations. Baltimore: Williams and Wilkins Company, 1940. \$4.00.

The fifth edition of this handbook covers the field of anaesthesia quite completely and presents detailed information about the management of the patient under general anaesthesia. The authors have done well to treat the subject, including the physiology of anaesthetics, the preparation of the patient and the techniques of administrations of anaesthetics, so briefly and at the same time to give the reader a working knowledge of the underlying fundamentals.

The anaesthetics are taken up in order, and cover in halothane, intravenous, rectal, local and spinal agents. The author places especial emphasis on ethyl chloride, chloroform, ether and nitrous oxide, since anaesthetists in England still use these more toxic agents. The newer agents and techniques that have been more recently introduced in that country, such as cyclopropane with carbon dioxide absorption anaesthesia, vinylene and the therapeutic use of oxygen, helium and carbon dioxide, are only briefly outlined.

In the section on local and spinal anaesthesia, there is quite a discussion of local agents and techniques and a very brief chapter on spinal anaesthesia.

There are many cuts of apparatus, many of which are different from those used in the United States.

The clinical anaesthetist and the medical student should find this book well worth reading. It gives a clear-cut picture of anaesthesia in England.

## NOTICES

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The forty-sixth annual meeting of the American Academy of Ophthalmology and Otolaryngology will be held at the Palmer House, Chicago, October 19 to 23.

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Alternating with the scientific programs of the section each afternoon will be an elaborate motion picture program. Thus when the section of ophthalmology meets for formal presentation of papers, motion pictures on otolaryngology will be available for those interested in that field.

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## THE TUFTS POSTGRADUATE MEDICAL PROGRAM

SAMUEL PROGER, M.D.\*

BOSTON

**M**OST postgraduate programs in operation today represent an attempt to continue the methods and technics of undergraduate instruction, making only what changes and modifications are required by the fact that the status of the practicing physician differs from that of the undergraduate. Much has been accomplished by this method, but perhaps more might be accomplished if the problem of postgraduate medical education were attacked not only from the standpoint of the school's relation to the practicing physician as a student, but also from the point of view of its relation to his hospital and his patients. Tufts College Medical School has attempted to do this.

In a sense, the problem of postgraduate medical education is the problem of the distribution of better medical care. Just as the fruitful attempt to solve the problem of undergraduate medical education has been largely responsible for the creation in this country of what are probably the world's highest medical standards, so conceivably could a comparably successful solution of the problem of postgraduate medical education assure the widespread utilization of the benefits of these high standards. Much vertical progress has been made, so that today American medicine, at least in its peaks, towers high. On the other hand, horizontal progress has been slow, and it must be admitted that our medical advances can be more widely, more rapidly and more effectively distributed.

Fundamentally, postgraduate medical education is, as the name implies, a union of the academic and clinical aspects of medicine. Logically, therefore, this union can best be maintained through an educational and clinical institution, that is, a medical-school and hospital center. During the last three years an attempt to develop such a fusion for the benefit of practicing physicians has been made by the New England Medical Center, which comprises Tufts College Medical School, the

Boston Dispensary, the Boston Floating Hospital and the Joseph H. Pratt Diagnostic Hospital. This work, so far experimental in nature, has been made possible by the Bingham Associates Fund, of which Dr. George B. Farnsworth is president.

The program has operated through three types of hospitals: the medical-school and hospital center, hospitals in regional centers and small community hospitals. The teaching facilities of each type of hospital are integrated into a single program. The teaching does not emanate from the central source alone. Rather, an attempt has been made to decentralize all activities as much as possible, in the effort to develop every local academic potentiality. Hence, one type of teaching is conducted through the central institution, another through the hospitals in the regional centers, and still another through the small community hospitals.

We have thought of the hospital as an instrument for teaching, regardless of its size or location. As each hospital becomes more of an educational institution, the standard of medical practice within it of necessity rises. This has been a well-nigh universal experience in hospitals that have assumed academic functions. What has been done in the past by medical schools for relatively large hospitals conveniently located to the school, Tufts now hopes to do for hospitals of various sizes, widely separated and distant from the academic center.

There are three general divisions of the program, divisions that to a large extent are interdependent and complementary. They are the Diagnostic Hospital Service, hospital extension services and postgraduate medical courses. Analysis will reveal that these divisions fit into a coherent educational design.

### DIAGNOSTIC HOSPITAL SERVICE

Those fortunate enough to be intimately associated with a teaching hospital are fully aware of the educational advantages of such an associa-

\*Professor of clinical medicine, Tufts College Medical School, medical director, Joseph H. Pratt Diagnostic Hospital

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to that which a clinical teacher in a hospital might give a house officer who, following a case work-up, desires advice and instruction. In this manner, the general practitioner in an isolated community may profit educationally from contact with a teaching institution.

A third educational feature consists in pertinent follow-up information. The hospital attempts to keep referring physicians informed of any important developments coming to its attention that may be of benefit to previously referred patients. For example, we have in the last several years seen a number of patients with parkinsonism. These patients were returned to their physicians with a recommendation for treatment by the more or less generally accepted method, with stramonium and scopolamine. Recent articles have appeared reporting good results in the treatment of parkinsonism with the use of the so-called "Bulgarian belladonna." An abstract describing this treatment was therefore sent to each of the physicians who had referred patients with Parkinson's disease. This abstract gave information about the drug and its use, with references to the published reports, for those who wished to obtain further details.

This type of critically filtered information has proved valuable, and it is our intention to extend its use still further, so that the practitioner in an outside community may come to feel almost as though he were on the active staff of the teaching institution.

Through the establishment of such an intimate relation between instruction and the actual care of patients, it is believed that Tufts College Medical School will inevitably increase the scope of its aid to its graduates, as well as to many other general practitioners.

A fourth educational feature of the Diagnostic Hospital Service is the *Bulletin*, which is published every other month and which contains clinical information derived from the various teaching activities at the New England Medical Center, particularly from the daily morning staff conferences at the Joseph H. Pratt Diagnostic Hospital. The *Bulletin* has an unusual appeal in that many of those physicians receiving it have been present at the morning conferences; and this familiarity, one may believe, is not only pleasantly reminiscent but is active in overcoming the customary lack of interest shown by medical men in material of this kind. To those who have attended the morning conferences as undergraduate or postgraduate students, the *Bulletin* represents an educational contact that makes continuous at least

one important phase of a past educational experience.

In addition to the four educational features of the Joseph H. Pratt Diagnostic Hospital listed above, we hope, at a future date, to provide at the New England Medical Center living facilities for those physicians who, through their local community, are in one way or another affiliated with us. Their occasional visits to Boston will thus bring them directly into an academic atmosphere, which should serve as a helpful and pleasant stimulus to their medical interests.

With the anticipated completion of full clinical facilities at the New England Medical Center, the central hospital part of our teaching program can be expected to become much more inclusive, along the lines indicated above.

#### HOSPITAL EXTENSION SERVICES

The hospital extension services are an important and at the same time unorthodox feature of our teaching program. These services are designed to make available improved hospital facilities for medical practice in the various communities concerned. It is clear that a postgraduate program that simply indicates to the general practitioner the value of improved laboratory, x-ray and electrocardiographic facilities, and then leaves him with no opportunity to avail himself of such aids, is not well rounded. A full educational program should take into consideration the hospital in which the physician practices, as well as the physician himself, and the possibilities for educational aid to those members of the hospital staff, non-medical as well as medical, whose services are auxiliary but without which modern medicine cannot be satisfactorily practiced. Such considerations led to the development of the hospital extension services.

These services are co-ordinated through the medical-school and hospital center, the hospitals in the regional centers and the small affiliated hospitals. The small community hospitals have their direct affiliations only with the regional centers, the regional centers being in turn directly affiliated with Tufts College Medical School and the New England Medical Center. At present, regional centers are located in Lewiston (Central Maine General Hospital) and Bangor (Eastern Maine General Hospital). The small hospitals affiliated with the Central Maine General are in Brunswick, Rockland, Bath, Damariscotta, Camden, Skowhegan, Waterville, Augusta, Farmington, Rumford and Boothbay Harbor. Those affiliated with the Eastern Maine General are in Greenville, Dover-Foxcroft, Belfast, Blue Hill, Cas-

tine, Bar Harbor, Machias, Lubec, Calais, Island Falls and Houlton. The plan of working with small hospitals through intermediary centers has proved most satisfactory, as indicated in a previous paper on the subject.\*

Services are now being offered in the fields of pathology, electrocardiography, radiology, laboratory aid, dietetics and library assistance. Briefly, these functions are as follows:

*Pathology.* Since pathology is a highly specialized subject, it is impracticable for physicians to practice part-time pathology as they may, for example, practice radiology. As a result, the small community hospital usually has no local pathologist. Under hospital extension services, all tissue specimens are routinely sent from the small hospitals to the regional-center hospital. An immediate report is sent back, by telephone when necessary, and all questionable specimens are sent on to the head of the Pathology Department at Tufts College Medical School, who is at all times available for consultation. On request, the pathologist in the regional center will gladly review all slides with the interested physician. In an increasing number of cases, furthermore, post-mortem examinations at the affiliated hospitals have been performed by the regional-center pathologist; this is a valuable indication of growing interest on the part of local practitioners. The regional-center pathologist is also available for clinicopathological conferences in the small communities.

*Electrocardiography.* A course of one week's duration in the interpretation of electrocardiograms is given to representatives of the community hospitals. The course is given without charge on the condition that the hospital purchase an electrocardiograph. Then, from the community hospitals, the local electrocardiographer sends a copy of every tracing to the electrocardiographer in the regional center, whose reports become available for check by the physicians in the community hospitals. The tracings that are unusually difficult to interpret are sent from the regional center to Boston, where several well-known cardiologists are available when necessary. In this manner, the small hospitals have available the best authorities on the interpretation of electrocardiograms, when they are needed. At the same time, the electrocardiographer at the small hospital is given constant opportunity for supervision and improvement.

The short course in electrocardiography thus serves as the beginning of a continued and per-

manent form of instruction. This principle is at once one of the most distinctive and most important features of our teaching efforts. Some of the other specialized courses recently given, such as in allergy and hematology, as well as to a large extent the regular courses in general medicine, pediatrics, obstetrics and gynecology, may all be taken as similar examples. This arrangement for postgraduate courses appears to have definite advantages over the customary method of simply offering, to whoever wants it, a course when he wants it. A course that is only an isolated cross-sectional experience in a physician's life is not likely to mean so much to him as one that is a regular part of his active professional career.

*Roentgenology.* Through a recently inaugurated plan, x-ray seminars are held every two weeks at the Eastern Maine General Hospital in Bangor. These are attended by the roentgenologists from the affiliated community hospitals, and traveling expenses are covered by the Bingham Associates Fund. All routine films are sent in advance to the regional hospital, so that consultation notes concerning them will have been dictated and the films of particular interest will have been chosen for discussion at the seminar. Thus, when the men meet, there is discussion of the problems with which they are immediately concerned, and of the general x-ray problems with which they should be kept familiar. This program serves not only as instruction to the doctor but also as a consultation service to the patient, a feature that is likewise significant in the pathological and electrocardiographic services. In addition, it has the advantage of giving the radiologist an opportunity to profit from the experience and material of ten hospitals instead of being limited to his own. In the interval between the seminars, emergency films may be sent in for examination, and the Bangor roentgenologist also makes occasional visits to the local hospitals to help them and to become acquainted with their equipment and facilities. The Bingham Associates Fund makes it possible for the regional radiologist to attend the weekly radiologic seminars at the Massachusetts General Hospital in Boston, which thus becomes, when necessary, a final court of appeal for the small hospitals, serving at the same time as a valuable source of instruction and education to the regional radiologist. The x-ray technicians in the small hospitals meet every second month at the Eastern Maine General Hospital in Bangor for a conference on their own problems. Fellowships for further study in Boston are available for them when needed.

In the Lewiston group, the regional radiologist visits the affiliated hospitals once a week, the pro-

\*Proger, S. The Joseph H. Pratt Diagnostic Hospital. *New Eng. J. Med.* 220:771-779, 1939.

gram otherwise being essentially the same as that of the Bangor group. Of the two, the Bangor plan seems to be more promising, since it is capable of reaching an unlimited number of hospitals in a large area, and geographical factors are minimized.

**Laboratory aid** Scholarships are granted to x-ray and laboratory technicians for advanced and specialized studies, chiefly in the laboratories of the Joseph H. Pratt Diagnostic Hospital. Technicians in each small hospital annually spend one month in Boston for the purpose of improving their technique and learning new methods and procedures. An itinerant technician is provided to substitute in the affiliated hospital for the duration of the course. During the fiscal year 1939-1940, twenty-seven such scholarships for technicians were awarded.

Last winter, in addition, a one-week course in chemistry was given by the chief chemist of the Joseph H. Pratt Diagnostic Hospital at the Central Maine General Hospital for the technicians of the Lewiston group. Attendance at its sessions was large, and demonstrations, appraisals and criticisms of methods were carried out.

In an attempt to standardize laboratory procedures, many of the hospital laboratories receive from the central laboratories solutions of the various reagents used in tests. By means of this arrangement, the number of variable factors is reduced, and accurate results are more easily obtainable in the small community hospitals.

Some of the affiliated hospitals are so small (10 to 20 beds) that they do not seem to require a full-time laboratory technician. No hospital is too small to have nurses, however, and we have therefore arranged for hospitals in this category to send one of their graduate nurses to Boston for a three-month period of instruction in the technique of performing a certain number of simple but important laboratory tests. Through such a course, and annual one-month courses thereafter, it is possible for a graduate nurse to perform, on a part-time basis, common laboratory tests in a small community. Arrangements have been made for the more difficult tests to be done in the regional centers.

**Dietetics** In dietetics, postgraduate study is made possible largely through scholarships, which enable the dietitians in the community hospitals to spend one month of each year regularly at the New England Medical Center, where they are given a continued course of instruction, through which they are kept informed of progress in their field.

**Library assistance** The Gerrish Library at the Central Maine General Hospital serves as a central library for the entire Lewiston group. It prepares bibliographies and sends out books for practitioners, as well as conducting a mailing service on current journals. The affiliated hospitals regularly receive selected current journals by this system. After four days, the journals are sent on to the next hospital, and new ones are received. The plan has received enthusiastic co-operation among the participating hospitals, and many libraries may well envy their record of not one journal lost during the year, although most of the journals have been consulted by many staff doctors.

In addition to these services now being offered, it is hoped that aid may in the future be given in the fields of nursing, anesthesiology and hospital administration.

In summary, then, it is clear that through a system of scholarships and direct hospital consultations a practicable method of continued education in certain auxiliary medical fields has been established. In pathology, instruction is given in the form of consultations and supervision of technical and diagnostic work by the professor of pathology at Tufts College Medical School. In roentgenology, the instruction involves supervision and consultation work by the roentgenologists in the regional centers, who in turn are enabled through a fellowship to attend the weekly seminars at the Massachusetts General Hospital. In laboratory work, the instruction is through annual scholarships for one month's actively supervised work at the New England Medical Center. A similar arrangement obtains in dietetics. In electrocardiography, the instruction in the small communities consists of routine consultations on all tracings, where as for the electrocardiographer in the regional center, instruction through consultation is available when necessary. In general, it is evident that there is opportunity for a free and automatic exchange of opinions between small communities, regional centers and the metropolitan teaching center.

#### *Teaching Ward Rounds*

Another feature of the extension service is aimed directly at the staff members of the affiliated hospitals, namely, teaching ward rounds. It is our belief that the best sort of extramural clinical teaching we can offer practicing physicians is such instruction as may be given through actual contacts with patients, as on ward rounds. Apparently the most satisfactory sort of instruction in general medicine that graduates obtain in their internships is that which they receive from the more or less informal discussions incident to ward rounds and directly related to cases and clinical

problems with which they have intimate association. Since this type of instruction has proved universally effective, it has seemed desirable to apply it in our own work. This we have done, with most encouraging results, by having instructors, chiefly members of our own staff, conduct teaching rounds once a month in the affiliated hospitals. In this manner, we are able to present an informal type of regular instruction that, it is fair to presume, offers much of value, if for no other reason than that it deals with timely and important local problems with which the local men are familiar. An informal discussion by a qualified instructor, in the course of such rounds, on how to treat John Smith (whom most of the local doctors know), who has a bleeding duodenal ulcer, is likely to produce a much stronger impact from the educational point of view than a formal discussion by the same instructor to the same group on the treatment of peptic ulcer.

Correspondence follow-up is applied to this ward-round instruction. The instructor who conducts the rounds sends, within the four weeks following his visit, an informal letter to each of the staff members of the community hospital, presenting some of the recent literature concerning the cases seen on rounds, offering critical comments, and summing up the most important points raised during the visit. In this manner, many of the case discussions on ward rounds are followed up by written instructions. With a different instructor to conduct teaching rounds each month, the staff members of the hospitals concerned receive written or oral instruction almost every other week throughout an academic year (eight or nine months), whereas the individual instructors are not too greatly burdened.

Some of the advantages of instruction through teaching ward rounds are as follows. A natural consequence of the meetings is that the local physicians whose cases are presented are stimulated to improve the quality of their case work-ups. References made to desirable procedures, facilities for which are lacking, in diagnosing or treating the cases under discussion occasionally prompt the staff and hospital to provide for such procedures in the future, thereby improving the entire local apparatus for diagnosis and treatment. A large number of our teaching staff are given an opportunity for intimate contact with most of the staff members of the affiliated hospitals, resulting in a wide diffusion of men and ideas. We are able further to utilize in our teaching program our hospital affiliations. We have the opportunity to offer instruction through what is generally considered the best possible medium, namely, a small

community hospital. We reach most of the physicians in the hospitals concerned. The effectiveness of this instruction is prolonged through the correspondence follow-up.

### POSTGRADUATE COURSES

These courses consist essentially of more or less orthodox short courses in various medical and surgical fields. They vary in duration from one to four weeks and are especially designed for general practitioners. Almost all the courses are given at the New England Medical Center.

Until 1940, only one-month courses were given. There are many reasons why courses of less than one month's duration are undesirable. In fact, even one month is not really long enough for truly adequate instruction in such fields as general medicine, pediatrics, obstetrics and gynecology. However, the more serious objections are avoided if these shorter courses are intended not to serve as complete instruction in any field, regardless of how limited that field, but rather as the beginning of continued instruction.

The advantages of longer periods of instruction are obvious. There are certain real disadvantages. First and foremost is the fact that such courses (one month or more) are at best taken by a relatively small number of physicians in a given area (about 10 per cent, in our own experience as well as in that of others). If by the nature of things only about 10 per cent of the physicians are reached by a given program, the program is automatically limited in its usefulness.

One month is longer than most physicians feel they can safely spend away from their practices. The fact that they can safely spend a month away is not nearly so important as the fact that 90 per cent of the physicians do not believe that they can, or have no desire to devote a month to additional training. The shorter courses would meet the objections at least of some of those who find a month too long.

The principal reasons, then, for instituting one-week courses, after having for three years given only those of one month's duration, may be outlined as follows. A greater number of men may be expected to leave their practices for one week than for one month. In a limited subject, much more concentrated and effective teaching can be given. The students are apt to be more interested in the instruction, since it will be directed toward a subject that they themselves have selected rather than one that covers a general field, many aspects of which may not be of particular interest to them. Experiences throughout the country have indicated that short, intensive courses are, by and

large, more satisfactory than longer ones. The subsequent correspondence, as outlined below, prolongs the effectiveness of such a course.

The courses themselves are, as mentioned above, essentially no different from those given in many schools throughout the country. Two features associated with this part of our teaching program, however, are not widespread and hence deserve some special mention. First, living quarters in the institution are provided for those taking courses. Our efforts have always been directed toward making the postgraduate student throughout his stay with us, and thereafter, if he wishes, an integral part of our organization. The fact that most of these students live with us during their course of study—and will be enabled to do so, we hope, on their repeated visits to Boston subsequently—has tended even further to integrate their work with that of the institution. Throughout their stay, they are constantly in a medical atmosphere, and live and mingle freely with residents, visiting staff and fellow students. This has proved of real value.

The second distinctive feature of this part of our program is the follow-up procedure, whereby physicians who have participated in a course are kept informed by letters from their instructors of new developments in the field covered by the course. These letters are sent out as new material of value to the practicing physician appears in the current literature to which he may not have access, or as new experiences develop that the instructors deem worthy of transmission to the physicians who have participated in their courses.

#### DISCUSSION

In formulating plans for a postgraduate medical program, it may be helpful critically to analyze past programs, many of which, although magnificent in conception, failed to achieve their aims. In these unsuccessful efforts, at least one fact stands out as a possible cause of ultimate failure, namely, that for success they were dependent on the voluntary and active co-operation of the practicing physicians. Widespread voluntary co-operation can be stimulated temporarily by an intensive campaign or it can be maintained locally by a forceful personality, but it cannot be ingrained, so that sooner or later the initial force subsidies, interest wanes, and the program collapses.

Any program, therefore, to be successful on a broad scale must be directed toward the development of a condition in which continual education will be automatic, regular and taken for granted. In other words, active interest and co-operation on the part of the student physician will not be a

prerequisite to initial work, but passive acquiescence alone will be necessary. Perhaps it is not too much to say that the majority of physicians are not interested in continued education when such education requires any undue application or even slight sacrifice. Indifference under such circumstances is unfortunately a widely prevalent human trait, and any program that presumes that higher motives can be made to prevail generally is doomed to failure.

Perhaps this point will indicate, on the other hand, at least some of the factors responsible for the comparatively wide success of undergraduate education. It appears that a fundamental condition in successful educational programs, such as undergraduate programs, is that, to acquire various benefits, certain requirements must be met by the student; and these demand consideration. Study is not made an end in itself, but rather a means to an end, to a definite and to a practically desirable end. Undergraduate educational programs assume that an altruistic goal is not capable of stimulating sustained effort or interest. Hence, we have diplomas, credits, degrees and so forth. These are but artificial and arbitrary goals set up to serve as prolonged stimuli for the production of sustained effort. Students work for four years toward a degree much more conscientiously than they study for enlightenment; they "work for a degree." Some such stimulating force is necessary to overcome normal human inertia, and to be permanently effective it must be permanently active. Why, if artificial stimulation is required for effective undergraduate education, should we assume that the field of postgraduate education can do without it? Actually, there is reason to believe that in older age groups some means is even more necessary for overcoming the human tendency to do nothing that is not required for an obvious and immediately desirable end. Those in the older groups at least have their time otherwise fully occupied.

What we have done has tended to make our teaching program so much a part of a physician's daily life that to some extent it has become automatic and continuous. We have thus far done little in the way of direct inducements. This we hope to do through plans now being developed for more direct affiliations between practicing physicians and the medical school, through the local hospitals, and also through regular opportunities for academic and professional recognition.

#### SUMMARY

The members of the faculty of Tufts College Medical School look on the problem of postgrad-

uate medical education as intimately bound up with the problem of the distribution of better medical care. They have therefore developed a postgraduate medical program that goes beyond the traditional relation of teaching institution to physician, to extend to that physician's hospital and to his patients as well. Thus, although the program includes postgraduate courses for practicing physicians, it is also concerned with improved hospital facilities, as well as diagnostic services, for those physicians, and through them for their patients.

The program functions through the medical school and affiliated hospitals of various sizes (small community hospitals, larger hospitals in regional centers, and the central, medical school and hospital center). What has been done in the past by medical schools for relatively large hos-

pitals conveniently located to the school, it is now hoped can be done for hospitals of various sizes, widely separated and distant from an academic center.

The program is divided into three parts: the Diagnostic Hospital Service, hospital extension services and postgraduate medical courses. In general, the attempt has been made to offer the medical student continued contact with his school throughout his medical career, through the medium of his local hospital and his patients, as well as through the customary postgraduate courses.

The program is so designed as not to interfere with existing educational activities, such as teaching clinics, community and other society meetings, staff meetings, medical-journal reading and so forth; it is intended rather to stimulate and supplement such activities.

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## CHLOROSIS\*

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**C**HLOROSIS, defined by Patek and Heath<sup>1</sup> as "a hypochromic anemia in adolescent girls and young women, usually associated with gastrointestinal and menstrual disturbances," is considered today a medical curiosity. In view of its frequency during the latter part of the nineteenth century and its rapid regression since then, "chlorosis seems destined to occupy only a niche in medical history rather than the prominent place among blood dyscrasias which it has held in the past."<sup>2</sup> It is extremely unlikely, however, that a disease etiologically dependent on universally current conditions such as growth, blood loss and inadequate diet should completely disappear. There is no doubt that chlorosis was quite frequent half a century ago. Its high incidence then, however, was more apparent than real. This is obvious from von Hoesslin's<sup>3</sup> critical analysis of 143 cases diagnosed as chlorosis. Of these, 64 had histories suggesting tuberculosis; 25, gastric ulcer; 13, psychoneurosis; 13, secondary anemia due to endocarditis or other infections; and 5, excessive blood loss. The remaining 23 cases might have been called "possible chlorosis." It is true, on the other hand, that chlorosis in severe form is rather uncommon at the present time. One of the factors responsible for the apparent rarity of the disease today is

the allocation of many mild and some severe cases of chlorosis into the categories of nutritional anemia or microcytic anemia with achlorhydria. Among Mills's<sup>4</sup> cases of idiopathic hypochromemia, for example, one twenty-six-year-old patient had been anemic for ten years. In McCann and Dye's<sup>5</sup> series of cases of chlorotic anemia with achlorhydria, one nineteen-year-old woman had been anemic for five years. These were probably cases of adolescent chlorosis.

Chlorosis, therefore, is not so rare today as has been implied. During the last four years, I have personally observed 8 cases. Three of these (Cases 1, 2 and 3) have been reported.<sup>6</sup> There was no clinical or laboratory evidence in any of these patients of acute, recurrent or chronic infections, severe visceral disease or abnormal blood loss.

## CASE REPORTS

**CASE 1.** A 19-year-old girl was seen in November, 1936, complaining of weakness, some shortness of breath, palpitation and vague pains in the lower abdomen. Born in Scotland, she had come to the United States at the age of 2 years. She was born at term and was of normal weight at birth. She received neither orange juice nor cod-liver oil during early infancy. Her appetite had always been capricious, and her diet grossly deficient in green vegetables and meats. At the age of 5, she was told that she was anemic and was given some medicine for the anemia; this she took for a short time. At the age of 10, she was told again by a physician that she was anemic; this time she took the prescribed medicine for about a month. Her

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menses had begun at the age of 14 and had always been very scanty, particularly during the previous year.

There was no history of any previous serious illnesses or operations.

On examination, the patient appeared well developed and plump. She had a temperature of 100°F by mouth. The skin was strikingly white, with a suggestion of a greenish tint. The face was definitely puffy. The scleras were not icteric. The mucous membranes of the mouth

CASE 2 A 19 year old girl was first seen by Dr. Frank Mirabello in November, 1936, when she complained of a mild head cold. She was born in Nova Scotia and had been in the United States for 3 years. She was born at term and had normal weight at birth. Her diet had always been adequate. Menstruation began at the age of 13, and the quantity, duration and recurrence of the menses had apparently been normal.

On examination, the patient appeared well developed,

TABLE 1 Initial Laboratory Findings in 8 Cases of Chlorosis\*

CASE NO.	HEMOGLOBIN	RED CELL COUNT	WHITE CELL COUNT	PLATELET COUNT	MCV	MEAN CORPUSCULAR VOLUME	PERCENT UNCLUSTERS	LYMPHOCYTES	MONOCYTES	EOSINOPHILS	TOTAL PROTEIN	ALBUMIN	CHOLESTEROL	ICTERIC INDEX	SERUM TITIN
	g	$\times 10^6$	$\times 10^3$	$\times 10^4$	f	f	%	%	%	%	g/100 cc	g/100 cc	g/100 cc		mm/hr
1 (1936)	52	4.92	10.8	167	17	1	69	16	11	4	5.6	3.1	2.5	5	10
(1938)	71	4.58	8.8	0	—	—	58	33	—	2	—	—	—	5	8
2	55	4.44	7.5	50	—	67	58	35	5	2	4.7	2.7	2.0	5	9
3	50	4.16	6.3	147	—	67	55	37	6	2	6.3	3.1	3.2	5	8
4	56	3.84	5.1	41	—	—	58	32	8	2	—	—	—	6	6
5	68	3.94	0	54	—	70	55	40	2	3	6.5	4.3	2.2	9	4
6	56	3.94	5.6	48	—	70	55	35	9	1	8.1	5.3	2.9	8	8
7	57	4.83	7.1	50	—	—	54	34	6	2	—	—	—	—	18
8	28	3.30	2	117	f	—	81	12	7	0	—	—	—	—	8

\*The stained blood films of all these cases revealed small pale red cells showing moderate anisocytosis and poikilocytosis. The films of Case 9 presented in add t on some rouleaux formation.

were very pale. The tongue appeared normal. The heart was normal except for a soft systolic murmur over the mitral area. Examination of the lungs, abdomen, pelvis and rectum was negative. The extremities were negative except for some prebital pitting edema. The fingernails appeared rather thin.

The urine and stools were normal. The blood Hinton reaction was negative. The other initial laboratory find

but rather thin. There was slight swelling and reddening of the mucous membranes of the nose, and some generalized injection of the throat. The temperature was normal. There was moderate pallor of the mucous membranes of the mouth. The tongue was normal. The heart, lungs, abdomen and extremities were normal, as were the fingernails.

The urine and stools were normal. The blood Hinton reaction was negative. The remaining initial laboratory findings are given in Table 1, and the results of the gastric analysis are shown in Table 2.

The patient was placed on 4 gr ferrous sulfate therapy thrice daily. At the end of 5 weeks, the red cell count was 5,330,000, and the hemoglobin 82 per cent (Sahl).

CASE 3 This patient, a twin sister of the patient in Case 2, presented a history identical with that given by her sister. She was seen first by Dr. Mirabello in November, 1936, when she complained of a mild upper respiratory infection. On examination, the patient appeared well developed and well nourished. There was slight swelling of the nasal mucous membrane, and slight red dening of the throat. The temperature was normal. There was moderate pallor of the mucous membranes of the mouth. The tongue was normal. Examination of the heart, lungs, abdomen and extremities was negative. The fingernails were normal.

The urine and stools were normal. The blood Hinton reaction was negative. The remaining initial laboratory findings and the results of the gastric analysis are presented in Tables 1 and 2.

Under ferrous sulfate therapy, in doses of 4 gr thrice daily, the red-cell count rose at the end of 5 weeks to 5,400,000, and the hemoglobin to 74 per cent (Sahl).

CASE 4 A 19-year-old American-born Jewish girl was seen in March, 1939, complaining of scanty menstruation. She was born at term and was of normal weight at birth. The past history was not significant. The diet had always been adequate. Menstruation began at the age of 14 and remained regular for 1 year. During the previous 3 years, the menses had been intermittently scanty, more particu

TABLE 2 Results of Gastric Analysis in Patients with Chlorosis

CASE NO.	FASTING		ONE HOUR AFTER TEST MEAL		ONE HOUR AFTER HISTAMINE INJECTION	
	UNITS OF ACID		UNITS OF ACID		UNITS OF ACID	
	Free	Total	Free	Total	Free	Total
1 (1936)	0	10	—	—	0	15
(1938)	0	10	—	—	0	10
2*	0	10	0	10	—	—
3	0	10	—	—	0	10
4	0	10	—	—	0	15
5	0	10	—	—	0	10
6	0	10	0	10	0	30
7*	0	5	0	5	45	55
8	0	15	—	—	12	35

\*G on a caffeine test meal.

ings are presented in Table 1, and the results of the gastric analysis are shown in Table 2.

The patient was given 4 gr ferrous sulfate thrice daily. At the end of 7 weeks the red-cell count was 4,700,000, and the hemoglobin 82 per cent (Sahl).

The patient felt fairly well for nearly 2 years. The duration and quantity of her menses had remained essentially normal during this period. She was seen again in September, 1938, complaining of fatigue. Physical examination was essentially negative. The urine and stools were normal. The laboratory findings are shown in Table 1, and the results of the gastric analysis in Table 2. The patient was again placed on ferrous sulfate therapy, 4 gr thrice daily. At the end of 6 weeks, the red cell count was 4,250,000, and the hemoglobin 82 per cent (Sahl).

larly during the previous 3 months. For the previous few weeks, the patient had had intermittent headaches. Three years previously, she was treated for a short time with iron for "secondary" anemia.

On examination, the patient appeared well developed, but rather thin. The scleras were not icteric. Examination of the eye grounds was negative. The mucous membranes of the mouth were pale. The tongue appeared normal. Examination of the heart, lungs and abdomen was negative. The fingernails were normal.

The urine and stools were normal. The blood Hinton reaction was negative. The remaining initial laboratory findings and the results of the gastric analysis are presented in Tables 1 and 2.

The patient was given ferrous sulfate, in doses of 4 gr. thrice daily. At the end of 3 weeks, the red-cell count was 4,050,000, and the hemoglobin 82 per cent (Sahli).

CASE 5. A 14-year-old girl was seen in November, 1938, complaining of cramps in one hand. Her parents were Irish. She was born at term and had normal weight at birth. The past history was not significant. Her appetite had always been capricious, and her diet deficient for years in meats and green vegetables. Catamenia began at the age of 14 and had always been irregular and scanty. One year previously, the patient had been treated for a short time with iron for "nutritional anemia."

On examination, the patient appeared fairly well developed but rather thin. There was moderate pallor of the mucous membranes of the mouth. The tongue was normal. Examination of the heart, lungs, abdomen and extremities was negative. The fingernails were normal.

The urine and stools were normal. The blood Hinton reaction was negative. The remaining initial laboratory findings are presented in Table 1, and the results of the gastric analysis are shown in Table 2.

At the end of one month's treatment with ferrous sulfate, in doses of 4 gr. thrice daily, the red-cell count was 4,590,000, and the hemoglobin 80 per cent (Sahli).

CASE 6. A 17-year-old girl was seen in August, 1938, complaining of a sore throat and pain in one knee of 2 days' duration. Her parents were Irish. She was born at term and had normal weight at birth. Her diet had been inadequate for several years in meats and green vegetables. Catamenia began at the age of 12, and the quantity, duration and frequency of the menses had apparently been normal.

The patient had had measles, pertussis, mumps and varicella. She had catarrhal jaundice at the age of 11. She was said to have had rheumatic fever at the age of 4, when she was in bed for 1 week.

Physical examination revealed a well-developed, pale girl. There was a definite greenish tint to the skin. She had an oral temperature of 100.2°F. There was moderate pallor of the mucous membranes of the mouth. The tongue was normal. There was mild generalized injection of the pharynx. The lungs were clear. The heart was normal in size; there was a short systolic mitral murmur. The rest of the examination, including that of the joints, was negative.

Examination of the urine was negative. Examination of the stools revealed a slightly positive reaction with the benzidine reagent on two occasions, but negative reactions on subsequent examinations. Woldman's<sup>7</sup> phenolphthalein test for enteric lesions was negative. X-ray examination of the chest was negative. Electrocardiograms revealed inverted P waves in Leads 2, 3 and 4, a finding that was suggestive of rheumatic heart disease but not of any acute

involvement. The blood Hinton reaction was negative. The remaining initial laboratory findings are shown in Table 1, and the results of the gastric analysis are given in Table 2.

The temperature became normal in a few days and remained so.

In this patient, a therapeutic trial with arsenic was made initially—formerly, arsenic was a popular remedy for the treatment of various anemias; its mode of action, however, still remains obscure. Its effects in this patient were disappointing, as shown in Figure 1. Fol-

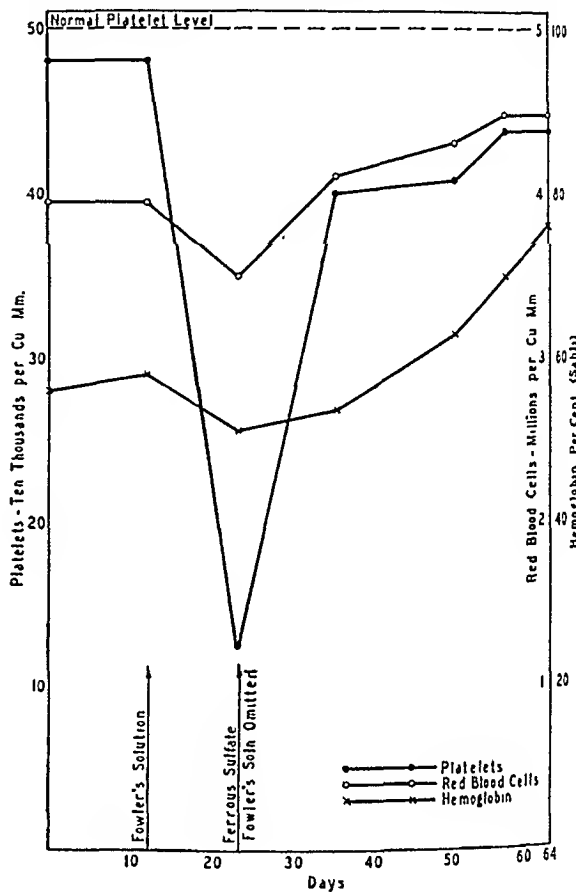


FIGURE 1. *The Behavior of the Hemoglobin and the Erythrocyte and Platelet Counts in Case 6 under Arsenic and Iron Therapy.*

lowing the administration of Fowler's solution in gradually increasing therapeutic doses, there was a decrease in the hemoglobin, erythrocyte and platelet values. The most impressive change occurred in the total thrombocyte count, which diminished in a short time almost to the critical level. The subsequent administration of iron, however, in the form of 4 gr. ferrous sulfate thrice daily, produced a satisfactory remission. At the end of 6 weeks, the red-cell count was 4,500,000, and the hemoglobin 85 per cent (Sahli).

CASE 7. A 22-year-old girl was seen in September, 1940, complaining of weakness, dizziness and anorexia of 1 year's duration. Her parents were born in the United States. She was born at term and had normal weight at birth. Her diet had been adequate. Catamenia began at the age of 14 and remained regular until 1 year before examination, when they became somewhat more frequent. There had been no change in the quantity of the menstrual flow. The past history was not significant.

On examination, the patient appeared well developed and well nourished. The mucous membranes of the mouth were pale. The tongue was rather small and slightly atrophic. Examination of the heart, lungs, abdomen and extremities was negative. The fingernails were normal.

Examination of the urine revealed the slightest possible

physician for observation because of unexplained anemia. His parents were of French-Canadian origin. He was born at term and was of normal weight at birth. His diet had been adequate. There was no history of any serious illnesses in the past.

Physical examination revealed a very well developed and well nourished boy. He had an oral temperature of

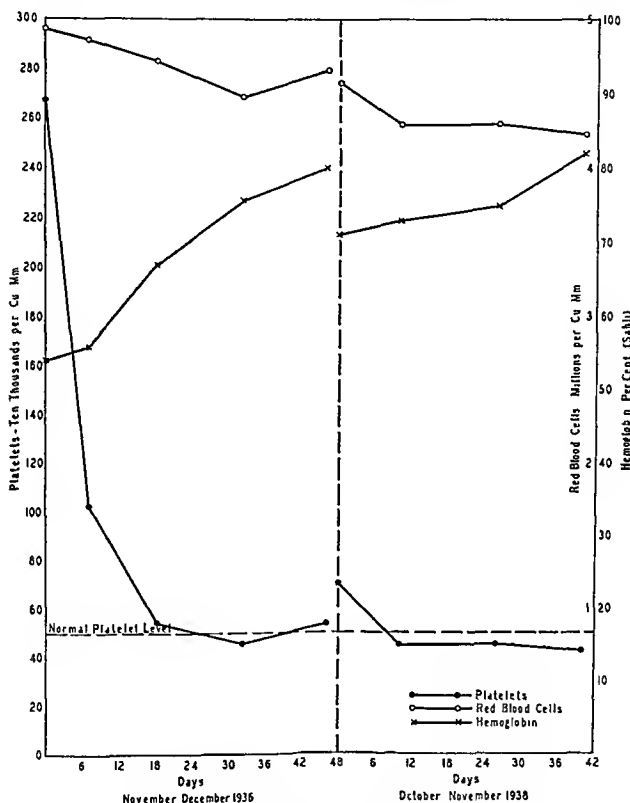


FIGURE 2 The Behavior of the Hemoglobin and the Erythrocyte and Platelet Counts in Case 1 under Iron Therapy

trace of albumin on one occasion. Renal function tests were negative, and the stools were normal. The blood Hinton reaction was negative. X-ray study of the chest was negative. The remaining initial laboratory findings are presented in Table 1, and the results of the gastric analysis are shown in Table 2.

The patient was given 4 gr ferrous sulfate thrice daily. At the end of 8 weeks, the red-cell count was 4,800,000, and the hemoglobin 87 per cent (Sahli).

CASE 8 A 16-year-old boy was seen in October, 1940. He had no complaints, and was referred by his school

100°F. There was a definite greenish tint to the skin, and a marked pallor of the mucous membranes of the mouth. The tongue was rather large and smooth. There was a loud systolic murmur over the mitral and pulmonic areas. The fingernails were thin, brittle, flattened and spooned.

The first urine examination showed a very slight trace of albumin, but subsequent examinations were negative. The first stool examination showed a slightly positive reaction with benzidine reagent, but subsequent examinations were negative. X-ray studies of the chest and the gastrointestinal tract were negative. Electrocardiograms

were normal. The blood Hinton reaction was negative. GastrosCOPY performed by Dr. Henry H. Lerner revealed evidence of acute and chronic gastritis. The other initial laboratory findings are shown in Table 1, and the results of the gastric analysis are presented in Table 2.

The patient was given 4 gr. ferrous sulfate four times daily. This was increased at the end of a week to six doses a day. At the end of 8 weeks, the red-cell count was 4,945,000, and the hemoglobin 85 per cent (Sahli).

### DISCUSSION

The anemia of patients with chlorosis is of the hypochromic microcytic type. The erythrocytes are flattened, small in size and poor in hemoglobin. An important and striking hematologic feature is thrombocytosis, which is not frequent, but which, when encountered, may be very marked. When thrombocytosis is present, the platelets undergo unusual quantitative changes after the institution of iron therapy. This behavior of the platelets is unique and very different from their behavior in other types of anemia under treatment, as I have pointed out elsewhere.<sup>6</sup> This is illustrated by Figure 2, which presents the hemoglobin levels and erythrocyte and platelet counts in Case 1. In November, 1936, the initial platelet count was 2,671,000 (normal count about 500,000<sup>8</sup>). Under iron therapy, the total thrombocyte count dropped promptly to approximately the normal level as the hemoglobin became elevated. Medication was discontinued at the end of about two months. When the patient was seen again in September, 1938, the platelet count was 700,000, and the hemoglobin 71 per cent (Sahli). The patient was obviously in mild relapse. Under iron medication, the platelet count again decreased to about the normal level as the hemoglobin values became elevated. The behavior of the thrombocytes in 1938, when the patient was in relapse, was the same, though not so spectacular, as in 1936. This inverse relation of the platelet values and hemoglobin levels represents an unusual hematologic finding. These quantitative changes in the platelets undoubtedly play a significant role in the development of the spontaneous venous thrombosis that is, at times, observed in these patients.

#### *Gastric Acidity*

Textbooks of medicine describe chlorosis as an anemia usually associated with either normal or increased acidity of the gastric contents. Many investigators, Naegeli<sup>9</sup> and Witts<sup>10</sup> among others, differentiate chlorosis from primary hypochromic anemia on the basis of the degree of the gastric acidity: in chlorosis, there is said to be an abundance of acid secretion in the stomach, and in primary hypochromic anemia there is usually an acidity. In

the literature, however, one finds an array of most conflicting reports describing isosecretory, hypersecretory and hyposecretory types. The most comprehensive report is that of Arneth,<sup>11</sup> who examined the gastric contents of 23 patients with chlorosis and found the total acid levels to be either normal or increased. However, careful analysis of the cases reported by this author reveals that the diagnosis of chlorosis can be seriously questioned in a number of cases. At least 5 of the patients had diseases that by themselves could produce anemia or could easily aggravate considerably a pre-existing anemia. Arneth's levels for the total acidity after a test meal ranged between 0.15 and 0.25 per cent in normal persons, and between 0.15 and 0.38 per cent in patients with chlorosis. At the present time, the normal ranges for gastric acidity are given as 0.4 to 0.5 per cent for free hydrochloric acid, and 0.4 to 0.6 per cent for the total acidity (Levinson and MacFate,<sup>12</sup> Wright<sup>13</sup> and Müller and Seifert<sup>14</sup>). Despite the fact that Arneth employed laboratory methods quite similar to those used now, the results he obtained were certainly low when compared with present standards. Considered from this angle, all his patients had hypochlorhydria. Furthermore, Arneth determined only the total acidity. In analyzing the gastric contents, it is essential to determine both free and total acidity. Decrease or absence of free hydrochloric acid is usually associated with a decrease in the total acidity and is indicative of either functional or organic disease of the parietal or oxyntic cells in the stomach. This type of deficiency assumes considerable significance in certain types of anemia, more particularly in pernicious anemia, primary hypochromic anemia, nutritional anemia in children and chlorosis.

Patek and Heath<sup>1</sup> were the first to carry out gastric analyses with histamine on patients with chlorosis. Of the 4 cases they reported, 1 patient had normal gastric acidity, 1 had marked hypochlorhydria, and 2 had complete achlorhydria. In other words, 50 per cent of their patients had complete histamine achlorhydria, and 25 per cent histamine hypochlorhydria. Of the 8 cases herein reported (Table 2), 4 had total histamine achlorhydria, 2 had hypochlorhydria after the injection of histamine, 1 had achlorhydria after a test meal, and 1 had hypochlorhydria after a test meal and normal acidity after the injection of histamine. In this latter group, therefore, 50 per cent of the patients had complete histamine an acidity, and 25 per cent had histamine hyp acidity.

The frequency of true histamine an acidity in normal adults is 10.8 per cent (Bloomfield and

Polland<sup>15</sup>). A review of the literature discloses that achlorhydria, even after the injection of histamine, is rather common among the very young (Klump and Neale,<sup>16</sup> Neale,<sup>17</sup> Vanzant et al<sup>18</sup> and Cutter<sup>19</sup>), then decreases rapidly in frequency, and remains low in incidence until about the age of twenty years. Between the ages of fifteen and twenty the incidence is very low (Vanzant et al,<sup>18</sup> 2.8 per cent; Wright,<sup>20</sup> 1.2 per cent; Bockus et al,<sup>21</sup> none; Polland and Bloomfield,<sup>22</sup> none). In other words, during the age periods when chlorosis is usually encountered, achlorhydria is rare. Therefore, the high incidence of histamine

of hemoglobin at a maximal rate than cases of hypochromic anemia without achlorhydria do. He also noted that small doses of iron often have essentially no effect in the achlorhydric patient, but frequently can cause a definite hemoglobin increase when the gastric acidity is about normal. Achlorhydria therefore reflects an abnormal state in the gastrointestinal tract that interferes with the liberation and absorption of the dietary iron and leads to a depletion of the iron stores in the body. As the demands on the hemoglobin and iron stores become increased, anemia appears. In chlorosis these new demands are due chiefly to

TABLE 3 Differential Features between Chlorosis and Primary Hypochromic Anemia

FEATURE	CHLOROSIS	PRIMARY HYPCHROMIC ANEMIA
Age	14 to 40 years	Usually 30 to 40 years
Symptoms	Those of anemia and of gastrointestinal and menstrual disturbances	In addition to those of anemia: sore tongue, dysphagia (Plummer-Vinson syndrome), paronychia and dermatitis
Skin	Texture normal; may present chlorotic or greenish tint; amount of pigmentation may be very scanty	Often dry and inelastic; may present abnormal pigmentation frequently fissures at the angles of the mouth
Hair	Normal	Frequently dry and prematurely gray
Fingernails	Usually normal	Frequently brittle, flattened, grooved and spooned
Tongue	Usually normal	Frequently atrophic
Splenomegaly	Rare; slight splenomegaly in 10 per cent of cases <sup>18</sup>	Frequent (in 50 per cent of cases <sup>23</sup> )
Blood	Leukocytes normal; occasionally increased; platelets normal; occasionally greatly decreased	Leukocytes normal or reduced; platelets usually reduced; occasionally normal <sup>24</sup>
Bone marrow	Normal <sup>14</sup> or hyperplastic <sup>14</sup>	Normoblastic hyperplasia <sup>25</sup>
Spontaneous venous thrombosis	In 2 to 3 per cent of cases <sup>18</sup>	None
Course	Remission without treatment; with permanent cure common	Spontaneous remissions rare

hypochlorhydria and achlorhydria found in patients with chlorosis must be considered one of the most characteristic features of this disease.

The free hydrochloric acid normally present in the stomach apparently affects ingested iron in two ways: it aids in the ionization of iron, and it prevents the formation of insoluble and undissociated iron compounds, particularly ferrous phosphate. The defective gastric secretion of the type observed in chlorosis must, therefore, play a role of some significance in the development of an iron-deficiency state. There is considerable evidence in favor of this view. Thus, Mettner and Minor<sup>23</sup> have shown that iron is more potent for blood formation when absorbed from an acid medium within the intestinal tract, rather than from an alkaline medium. Kellogg and Mettner<sup>24</sup> have observed that in some anemias due to chronic blood loss from peptic ulcer the alkalization process associated with a Sippy regimen inhibits the absorption of iron contained in the food. The iron balance studies of Fowler and Brer<sup>25</sup> indicate that achlorhydria interferes with the absorption of iron. Minor<sup>26</sup> has observed that cases of idiopathic hypochromic anemia with achlorhydria usually require distinctly larger doses of iron for the regeneration

growth and menstruation (Heath and Patek,<sup>1</sup> 27 Heath<sup>28</sup>). According to this hypothesis, chlorosis is a deficiency disease conditioned in many cases by a disorder of the gastrointestinal tract.

Since the growth factor is equally operative in both sexes, one would expect to find occasional cases of chlorosis among males. Allbutt<sup>29</sup> and, more recently, Witts<sup>30</sup> have described the disease in the male sex. The latter investigator reported 5 cases; the diagnosis in 2 cases, however, is doubtful. Case 8 of the series reported here represents a striking case of male chlorosis.

### Differential Diagnosis

There has been considerable diversity of opinion regarding the possible relation between classic adolescent chlorosis, summarized recently by Heath,<sup>28</sup> 32 and primary hypochromic anemia (also called "idiopathic hypochromic anemia," "simple achlorhydric anemia," "cryptogenic achylie chlor anemia," "chronic chlorosis" and hypochromic gastrogenous anemia), first clearly defined by Faber<sup>32</sup> and described more recently in detail by Heath and Patek,<sup>27</sup> Witts,<sup>33</sup> Dameshek,<sup>34</sup> Minor<sup>35</sup> and Wintrobe and Beebe.<sup>36</sup> Thus, Naegeli<sup>3</sup> and Witts<sup>30</sup> are of the opinion that, in the absence of

achlorhydria and dysphagia, the microcytic hypochromic anemia of middle-aged women is allied to adolescent chlorosis. Heilmeyer<sup>37</sup> believes that of the two primary iron-deficiency states, *chlorosis* and primary hypochromic anemia, the former is associated with atony of the stomach and ptosis leading to defective iron absorption, and the latter with a chronic change in the gastrointestinal tract. Adamson and Smith<sup>38</sup> and Bloomfield<sup>39</sup> maintain that chlorosis and primary hypochromic anemia are the same disease. Of course, it is possible that the clinical picture of chlorosis has been altered and that the relatively recently recognized syndrome called "primary hypochromic anemia" is really not a new type of anemia, but rather an example of modified chlorosis. In fact, some authors do speak of present-day or latter-day chlorosis (Mills,<sup>40</sup> Schulten<sup>41</sup>). It seems to me, however, more reasonable to consider chlorosis as a definite disease entity, a view entertained by many observers, Heath and Patek<sup>1, 27, 28, 31</sup> and Minot<sup>35</sup> among others. It occurs in two forms, a severe one, which is rather infrequent, and a mild one, which is, according to Heath and Patek<sup>27, 28, 31</sup> and Davidson, Fullerton and Campbell,<sup>42</sup> quite common. It presents a number of characteristic features differentiating it from primary hypochromic anemia, as shown in Table 3. It must be admitted that atypical cases of both conditions are occasionally encountered that seem indistinguishable.

#### SUMMARY AND CONCLUSIONS

Classic adolescent chlorosis has not disappeared; and since histamine anacidity or hypoacidity is a common finding, it is probably a deficiency disease conditioned by a disorder of the gastrointestinal tract. In chlorosis, the red cells are hypochromic, small and flattened. The thrombocytes quantitatively are normal or increased. In other types of anemia, such as pernicious anemia, primary hypochromic anemia and anemia due to acute and chronic blood loss, the number of platelets is reduced and rises with improvement of the anemia. In chlorosis, on the other hand, there is an inverse relation between the platelet level (when elevated above normal) and the hemoglobin value. When the thrombocytosis is marked, it is a very significant, if not an essential, factor in the production of spontaneous venous thrombosis at times observed in these patients. Iron therapy cures the disease.

The term "chlorosis" should be discarded. The disease is more appropriately called "hypochromic iron-deficiency anemia of adolescence, frequently associated with achlorhydria."

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## IMPERFORATE HYMEN WITH HEMATOCOLPOS\*

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**I**MPERFORATE hymen with hematocolpos, an infrequently encountered condition, may present difficulty in diagnosis and is not without danger in treatment.<sup>1-3</sup> In 1939, Tompkins<sup>4</sup> collected 113 cases from the literature and noted that there had been deaths in 6 cases and severe pelvic infections in 9; he added 5 cases, with a single fatality and an additional case of pelvic infection. It is the purpose of this paper to add to the literature 7 cases seen and treated at the Peter Bent Brigham Hospital from 1914 through 1940, certain diagnostic and therapeutic features are re-emphasized

### CASE REPORTS

**CASE 1** R. S., an 18-year-old girl, was admitted on December 4, 1914, complaining of back pain of 6 months' duration. Although the patient had been married for 5 months, coitus had never been successful. She had never menstruated. For 2 months, the pain had become severe, and was noted in the lower abdomen. She had had several bouts of urinary retention lasting 1 or 2 days.

Examination showed a young woman with well developed secondary sexual characteristics. There was a slightly rounded, tender, fluctuant, lower abdominal mass rising just above the umbilicus. The hymen was imperforate and bulging, and carried an impulse from the abdominal mass. By rectum, a vaginal mass was palpable.

At operation, the hymen was incised under ether anesthesia, and approximately 750 cc of reddish brown, viscid fluid evacuated. This was not cultured. A small uterus and normal vaults were palpated. The patient was afebrile after operation, and was discharged on the 7th postoperative day.

Three years later, in 1917, the patient was seen in the Outdoor Department. She reported normal periods, and had borne a child 1½ years previously.

**Comment** A normal pregnancy took place in a patient whose treatment was long delayed.

**CASE 2** H. H., a 14-year-old girl, was admitted on August 21, 1931, complaining of intermittent lower abdominal pain of 2 years' duration. The attacks came at approximately monthly intervals and lasted 5 to 7 days.

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the pain included the lower back. She had never menstruated, nor had she had any urinary symptoms.

Examination showed a slightly obese young girl with normal secondary sexual development. There was an indefinite, slightly tender, midline, lower abdominal mass. The hymen was imperforate. By rectum, a large fluctuant mass was palpable.

At operation, the hymen was excised under ether anesthesia, and a large amount of thick, "mucinous" old blood released. Culture was negative. The patient was afebrile after operation and was discharged on the 15th postoperative day.

Six months later, an examination in the Outdoor Department showed her to have a small normal uterus and cervix. In January, 1941, 9 years later, she reported normal and regular menstruation, although married for 1½ years, she had not become pregnant.

**Comment** A return of normal function followed drainage.

**CASE 3** R. J., a 13-year-old girl, was admitted on November 10, 1937. For about 4 months, she had noted increasing abdominal distention, and for 2 months she had had some lower abdominal pain, chiefly in the right lower quadrant. During this period, she had also experienced some difficulty in starting urination. She had never menstruated.

Examination showed a well developed young girl with normal secondary sexual characteristics. There was a fluctuant, lower abdominal, midline tumor resembling an overdistended bladder, but persisting after catheterization. The hymen was imperforate and bulged slightly when pressure was exerted on the abdominal mass. By rectum, a transmitted fluid wave from the abdominal mass could be palpated, but there was not a marked bulging of the vagina.

At operation, the hymen was incised under ether anesthesia, and 900 cc of chocolate-colored viscid fluid evacuated. The vagina was irrigated with saline. Culture of the fluid was negative. The patient was placed on constant urethral drainage for 6 days, remained afebrile, and was discharged on the 9th postoperative day. A questionable nodule of cervix was the only portion of the internal genitalia that could be palpated.

Following operation, the patient never established a normal menstrual cycle, although her sexual development was in other respects normal. Her periods were scant and irregular, with intervals of amenorrhea lasting as long as 4 months. The flow was usually "watery" blood lasting only a few hours, although recently (December, 1940) she

had a 3-day flow with clots. A course of injections with one of the anterior pituitarylike hormones had no appreciable effect. The patient also suffered from vague abdominal pain, chiefly in the flank; this could never be explained, even after several readmissions for study, and a complete urologic investigation.

**Comment.** This patient may still develop a normal menstrual cycle; if not, one must suppose that the uterus was so damaged that it is incapable of normal menses. There is no evidence that the ovaries do not function.

**CASE 4.** N.G., an 11-year-old girl, was admitted on July 7, 1938. This patient, one of twins, had had a foul-smelling vaginal discharge for several weeks. Her twin sister had had 3 normal menstrual periods, whereas she had had none. There had been no abdominal pain or urinary symptoms.

Examination showed a well-developed young girl with normally developed secondary sexual characteristics. The abdomen was normal. The hymen was imperforate except for a pin-point opening just beneath the urethral orifice, from which pus could be expressed by pressure through the rectum. Fullness in the vagina was palpable by rectum.

Under ether anesthesia, a thick hymen was incised and a pint of thick, foul-smelling pus evacuated. The vagina was irrigated with saline. Culture of the pus yielded a mixed growth of *Staphylococcus aureus*, *Streptococcus hemolyticus* and *Escherichia coli*. A normal-sized uterus and normal vaults could be palpated. The patient was discharged, afebrile, on the 1st postoperative day, to receive vaginal irrigations and protargol suppositories at home.

Follow-up in January, 1941, 2½ years later, revealed that the patient was having regular, painless periods lasting 4 days.

**Comment.** The problem presented by this patient differed from that in the usual case, inasmuch as infection from below had taken place. Local immunity was already well established, and the treatment became that of any well-localized abscess. There was no need for a long hospital stay, and vaginal irrigations had a definite usefulness.

**CASE 5.** M.R., a 14-year-old girl, was admitted on August 30, 1939. For 3 days, she had had pain in the rectum, and for 2 days she had had progressively severe lower abdominal pain. She had never menstruated.

Examination showed a well-developed young girl. There was a tender suprapubic mass rising halfway to the umbilicus. The hymen was imperforate, thin and bulging. A tender, boggy mass was palpable anteriorly by rectum.

Without anesthesia, but with careful preparation of the vulva, the hymen was incised in the Outdoor Department, and 450 cc. of dark blood released. This was not cultured. The patient was admitted to the hospital for observation, and was discharged 36 hours later.

Four weeks later, a normal-sized uterus could be palpated by rectum. In February, 1941, about 18 months after operation, the patient reported periods occurring regularly every 28 to 30 days, lasting 4 to 7 days, and occasionally accompanied by lower abdominal pain.

**Comment.** The intern who cared for this patient evidently had no understanding of the potential dangers to which he was subjecting her. It was fortunate that there was no postoperative infection. A normal menstrual cycle resulted after drainage.

**CASE 6.** M.N., a 15-year-old girl, was admitted on February 22, 1940, complaining of increasingly severe lower abdominal pain of 4 days' duration. She had never menstruated or had any urinary symptoms.

Examination showed a thin, young girl with normal secondary sexual development. There was a soft, rather tender, lower abdominal mass rising halfway to the umbilicus. The hymen was imperforate and bulging. By rectum, a tender mass was felt anteriorly.

At operation under ether anesthesia, the hymen was excised and 1000 cc. of chocolate-brown old blood evacuated. Culture of this was negative. A small normal uterus and normal vaults were palpated. The patient remained afebrile after operation and was discharged on the 11th postoperative day.

In September, 1940, 6 months after operation, she reported regular, normal, painless periods lasting 6 days. Examination showed that the hymenal opening had contracted to a size of 5 mm.

**Comment.** A return of normal function followed drainage. The introitus requires further surgical opening, in spite of the supposed excision of the hymen at the time of operation.

**CASE 7.** M.L., a 15-year-old girl, was admitted on August 9, 1940, complaining of constipation, back pain and aching down the anterior thighs for the preceding 7 months. She had never menstruated or had any urinary symptoms.

Examination showed a thin young girl with normal secondary sexual development. The abdomen was normal. The hymen was imperforate and bulging. An anterior mass was palpable by rectum.

Under gas-oxygen anesthesia the hymen was incised and 500 cc. of chocolate-colored thick fluid with some clots evacuated. *Bacillus subtilis* was cultured from this, but was regarded as a contaminant. No uterus or masses could be palpated. After operation, the patient remained afebrile and was discharged on the 10th postoperative day.

Five months after operation (January, 1941), she was seen in the Outdoor Department. A small uterus could be palpated by rectum. The hymenal opening was small. The patient reported regular, normal, painless periods every 28 to 30 days.

**Comment.** A return of normal function followed drainage.

### SYMPTOMS, SIGNS AND DIAGNOSIS

Imperforate hymen with hematocolpos occurs in girls between the ages of eleven and eighteen years. The symptoms are a direct result of the accumulation of menstrual blood behind the imperforate hymen. An invariable feature of the history is the fact that the patient has never menstruated; yet, curiously, although understandably, this all-important information is rarely volunteered and is never a prominent symptom. The usual presenting complaint is lower abdominal pain, which is commonly associated with pain in the lower back and occasionally in the rectum or anterior thighs. The pain is often crampy and may be severe. It may occur at intervals corresponding to the time of the presumed menstrual periods (Case 2). As shown in Table 1, abdominal pain was a presenting symptom in 5 of



the cases reported in this paper, although in one (Case 1) pain in the back and in another (Case 5) pain in the rectum seemed equally important. It is noteworthy that although all 5 of these patients had an easily palpable abdominal mass, not one had apparently attached any significance to it, even if she had noticed it.

Difficult urination or even complete urinary retention frequently occurs in these cases.<sup>1</sup> Only

patients should be hospitalized both for the operative procedure and for a postoperative period of ten to fourteen days. The operation must be carried out with scrupulous asepsis. Simple but generous incision of the bulging hymen may be sufficient, but if the hymen is thick and tough, excision may be preferable. A careful irrigation of the vagina in the operating room is probably without danger, but irrigations and douches must

TABLE 1 Summary of 7 Cases of Imperforate Hymen with Hematocolpos

CASE NO	AGE	DURATION OF SYMPTOMS	ABDOMINAL PAIN	COMPLAINTS BACKACHE	DIFFICULT URINATION	ABDOMINAL MASS	RESULT†
1	18	6 months	Yes	Yes	Yes	Yes	Normal menses pregnancy
2	14	2 years	Yes	Yes	No	Yes	Normal menses
3	13	4 months	Yes	No	Yes	Yes	Scant and irregular menses
4	11	3-4 weeks	No*	No	No	No	Normal menses
5	14	3 days	Yes	No	No	Yes	Normal menses
6	15	4 days	Yes	No	No	Yes	Normal menses
7	15	7 months	No	Yes	No	No	Normal menses

\*The only complaint was a foul vaginal discharge.

†All cases treated by incision or excision of the hymen.

2 of the reported patients (Cases 1 and 3), had urinary symptoms, and in neither were they prominent.

A careful physical examination cannot fail to establish the diagnosis. If a vaginal and rectal examination is invariably performed on girls or young women complaining of abdominal pain or difficult urination, cases of imperforate hymen with hematocolpos will not be overlooked, and cases in which the diagnosis is made only after laparotomy for real or supposed appendicitis,<sup>2,3</sup> or after cystoscopy,<sup>4</sup> will be prevented. It is unfortunate that in this age group the physician most easily persuades himself that such an examination is undesirable and probably unnecessary. In most cases, there will be a visible bulge at the introitus. An error may be made in regarding a small normal hymenal orifice as imperforate if it is concealed by overlying folds of mucosa, but a probe will demonstrate an opening if present. By rectum, the blood-filled vagina will be felt anteriorly as a boggy mass. There will usually be a slightly tender, rounded, lower abdominal midline mass, contiguous with the vaginal mass.

#### TREATMENT

The treatment consists in surgical drainage through the vagina of the dammed-up menstrual secretions. These patients, however, are particularly susceptible to ascending infection, introduced from without, which may produce a fatal pelvic cellulitis or peritonitis. Such an infection may have its onset days or even weeks after surgical drainage, as shown by reported cases. Because of this special danger from sepsis, these

not be used in the postoperative period. After the fluid has been evacuated and while the patient is still under anesthesia, a rectal, rather than vaginal, examination should be performed to determine the presence of palpable adnexal masses. If such masses are found, an immediate exploratory laparotomy should be considered, as suggested by Tompkins,<sup>1</sup> to remove or drain the blood-distended tubes.

In the postoperative period, the points to be stressed are bed rest in Fowler's position and the maintenance of strict perineal cleanliness. Some surgeons advocate a constipating regime for four or five days, although this does not appear to be necessary. A short course of sulfanilamide as a prophylactic is worthy of consideration. No restrictions on patients are required, once the period of hospitalization is over. Nevertheless, it is sound practice to advise against douching, tub bathing or vaginal examinations until two menstrual periods have passed, as urged by Tompkins.<sup>1</sup>

#### PROGNOSIS

The possibility of a fatal ascending infection has been pointed out; this should be avoidable with the exercise of sufficient care. Most of these patients start a normal menstrual cycle, and some go on to child bearing. The oldest patient (Case 1) in this group, aged eighteen, in whom one would naturally expect the severest damage to the uterus and tubes, bore a child eighteen months after operation. On the other hand, another patient (Case 3), aged thirteen at operation, subsequently had irregular and very scanty periods. One should neither be too pessimistic

with the late case, nor promise too much with the early one.

### SUMMARY

Imperforate hymen with hematocolpos is a syndrome occurring in girls between the ages of eleven and eighteen who have never menstruated. The usual presenting symptom is abdominal pain, often associated with back pain. There may be a history of difficulty in urination. The diagnosis is established by demonstrating the imperforate hymen, which is often bulging, and by palpating the blood-filled vagina through the rectum. There is usually an associated suprapubic mass.

Treatment consists of vaginal drainage of the dammed-up blood by incision or excision of the hymen under the most scrupulous asepsis; if adnexal masses persist after drainage, an immediate laparotomy for further surgical treatment of the tubes must be considered. The postoperative regimen consists of rest in bed in Fowler's

position for ten to fourteen days, strict perineal cleanliness and postponement of douches, tub baths and vaginal examination until several menstrual periods have passed. The prognosis for a normal menstrual cycle is good; normal pregnancies are known to occur.

Seven cases seen and treated in the Surgical Service of the Peter Bent Brigham Hospital from 1914 through 1940 are reported. There were no postoperative infections in this group, and no deaths. One patient is known to have had a subsequent normal pregnancy.

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## THE SIGNIFICANCE OF A HISTORY OF ASTHMA WITH REFERENCE TO SEROTHERAPY\*

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A RECENT circular letter<sup>1</sup> prepared by the Committee on Chemotherapeutic and Other Agents and the Subcommittee on Infectious Diseases, of the Division of Medical Sciences, National Research Council, included a discussion of the contraindications to the use of serum in patients with a history of allergic manifestations. The circular letter stated, "Serum should never be given to patients who have a history of asthma of any type or to those who have a history of hay fever." Because the circular letter carries the weight of authority, the statements contained in it are likely to influence treatment of the civilian population, as well as that of members of the armed forces. Since the sentence quoted was at variance with the impression gained from a previous study of reports on the use of antipneumococcus horse serum in New York State, it was considered appropriate to subject these reports to careful analysis regarding the point at issue. This seemed particularly im-

portant because a thorough review of the literature concerning immediate serum reactions in man failed to reveal any study comparing the incidence of immediate serum reactions in patients with and without a history of asthma.

In the review of the literature, no case of a death associated with a reaction to antipneumococcus horse serum in an asthmatic patient was found. Bullova<sup>2</sup> reported 8 fatal cases following the injection of antipneumococcus horse serum, none of which had a preceding history of asthma, and Heffron<sup>3</sup> reported 2 fatal cases, neither of which had a history of allergy preceding the injection of the serum. Heffron<sup>4</sup> also reported, "In the course of the Pneumonia Study and Continuing Program in Massachusetts, at least 15 patients with a history of asthma and 2 with a history of hay fever were treated without unfavorable reactions."

Between January 1, 1937, and March 31, 1939, 3215 reports on the use of antipneumococcus horse serum in which information of the history of allergy was recorded were received by the New York State Department of Health. Of these, 101 (3.1 per cent) indicated a history of asthma, although

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in no case was the asthma related to a history of specific sensitivity to horse emanations. This study must not be interpreted to include patients with a history of specific sensitivity to the animal from which the serum was derived.

As shown in Table 1, the incidence of immediate

TABLE 1. Incidence of Reactions Among Pneumonia Patients Treated with Specific Antipneumococcus Horse Serum, according to History of Asthma

GROUP	HISTORY OF ASTHMA		NO HISTORY OF ASTHMA	
	NO OF CASES	PER CENT	NO OF CASES	PER CENT
Thermal reaction	24	24.7*	515	16.5
Circulatory reaction	10	9.1*	117	3.8
Anaphylactic reaction	17	22.6*	227	7.3
Miscellaneous reactions	13	17.3*	2.8	8.9
Cases with reaction	46	45.5	922	29.6
Cases without reaction	51	50.5	2102	67.5
Cases unknown as to reaction	4	4.0	90	2.9
Totals	101		3114	

\*Adjusted to allow for older age distribution in cases with history of asthma.

serum reactions in the patients with asthmatic histories was greater (45.5 per cent) than that in those without such histories (29.6 per cent). This difference was found to be most significant in those patients having the anaphylactic type of reaction. However, the incidence of fatal reactions

TABLE 2. Incidence of Fatal Reactions Among Pneumonia Patients Treated with Specific Antipneumococcus Horse Serum, according to History of Asthma

GROUP	NO OF CASES	FATAL REACTIONS
Cases with history of asthma	101	1† (1.0%)
Cases with no history of asthma	3114	22 (0.7%)
Total	3215	23 (0.7%)

†This patient was sixty-five years of age with a long-standing history of cardiovascular disease and a three-year history of asthma. The conjunctival and intradermal tests were negative and he received 1 cc of serum intravenously without reaction prior to the fatal dose. The reaction was circulatory in nature.

was approximately the same in both groups of patients (Table 2). These data suggest caution

In a study recently published elsewhere<sup>8</sup> of 25 patients with fatal serum reactions and 790 with nonfatal immediate serum reactions of all degrees of severity, it was shown that immediate reactions following the injection of antipneumococcus horse serum can be divided into four categories: thermal, anaphylactic, circulatory and miscellaneous, the clinical pictures of which are defined. In that study all but one of the fatal serum reactions were shown to be circulatory in nature and not related to recognizable protein hypersensitivity.

in the administration of serum to asthmatic patients, but do not appear to justify the prohibition of its use in those patients with asthma not related to specific animal protein sensitivity.<sup>8</sup>

Further evaluation of the importance of asthma can be derived from a study of the fatality rates of serum-treated pneumonia patients according to asthmatic status. The fatality rates of patients with and without asthmatic histories did not significantly differ from each other after correction for differences in age and bacteremia (Table 3).

TABLE 3. Case Fatality Rates Among Pneumonia Patients Treated with Specific Antipneumococcus Horse Serum, according to Incidence of Reactions and History of Asthma

GROUP	HISTORY OF ASTHMA		NO HISTORY OF ASTHMA	
	NO OF CASES	% OF DEATHS	NO OF CASES	% OF DEATHS
Cases with reaction	46	12 (17.5%)	922	1.8 (13.9%)
Cases with no reaction	51	15 (14.4%)	2102	318 (15.1%)
Cases unknown as to reaction	4	0	90	16 (17.8%)
Totals	101	27 (16.8%)	3114	462 (14.8%)

†Adjusted to allow for older age distribution and larger proportion of positive blood cultures in cases with history of asthma.

Moreover, the mortality rates from pneumonia among patients with or without a history of asthma were not significantly different whether or not immediate serum reactions occurred.

In view of these findings, and in the absence of contradictory data in the medical literature, it is fair to conclude that a history of asthma due to other than specific sensitivity to the animal from which the serum is derived is not an absolute contraindication to serum therapy.

It is recognized that injection of horse serum may cause sensitization which increases the dangers of its subsequent administration. However, no evidence can be found in the literature that persons with hay fever or asthma are more easily sensitized with horse serum or rabbit serum than normal persons. Since our series does not contain enough patients who had received serum previously, we are unable to settle this point.

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Following a severe injury, so-called "primary shock" frequently occurs. This is really a condition of vascular collapse, in which the tone of the peripheral vessels is diminished reflexly, as a result of nervous or psychic stimuli. The vascular bed is dilated to such an extent that the volume of blood becomes insufficient to maintain an adequate venous return to the heart, and thus an adequate output to the periphery. It may be difficult to distinguish this form of collapse from true secondary shock; therefore, all patients admitted with a feeble pulse and lowered blood pressure should be treated immediately for collapse. This treatment involves administering morphine if there is pain, getting the patient warm with blankets and sometimes hot fluids (tea, of course, in England), and putting the patient in shock position with the feet elevated, because gravity plays such an important part in the pooling of blood. If the patient does not quickly improve under these conditions, true secondary shock is probably present.

Most workers agree that in secondary shock there is an insufficient volume of blood to maintain an adequate peripheral circulation, not because of vasodilation (vasoconstriction is usually present), but because of loss of blood or one of its components. This deprivation may come about in a number of ways. In extreme dehydration as in diabetic acidosis or severe diarrhea, it is caused by a loss of water and electrolytes. On the other hand, in hemorrhage it results from a loss of blood, and in burns or severe trauma it results from the oozing of plasma into the injured area. The immediate effects are concentration of those elements of the blood that are not lost, vasoconstriction, manifested by a cold and clammy skin and a thready pulse, and the subjective symptoms of sweating, thirst, anxiety and nausea. If the state of shock continues long enough, general capillary damage may occur, with leakage of plasma throughout the body, thus further exaggerating the symptoms.

In burns and crushing injuries with marked concentration of the red cells, the treatment of choice is the restoration of the lost plasma. Saline infusions are at best of temporary benefit, since the fluid is rapidly lost from the circulation, thus aggravating the condition by sweeping out the proteins of the blood, which are so necessary for the maintenance of its osmotic pressure.<sup>3</sup> On the other hand, in hemorrhage, the ideal therapy is the replacement of whole blood, since both red cells and plasma have been lost. In normal persons, there is a considerable margin of safety in

circulating hemoglobin, and the patient with an acute hemorrhage develops symptoms from diminished blood volume far sooner than from loss of hemoglobin. Hence, any form of therapy that restores the volume of blood and enables the remaining hemoglobin to circulate adequately is sufficient. After a hemorrhage, the concentration of hemoglobin is little altered at first, but gradually falls as the blood volume is brought back to normal by the production of plasma from the patient's own reserves.<sup>4</sup> However, when the hemoglobin falls below a certain level, this process of hemodilution proceeds only to a certain point.<sup>5</sup> Therefore, when a relatively low hemoglobin value is found to begin with, it seems unwise to administer plasma alone. British experience has borne this out. Whereas plasma is extremely effective in the treatment of most air-raid casualties, its use in the treatment of a small series of patients with bleeding ulcers whose hemoglobins were 50 per cent or less before treatment was frequently accompanied by reactions and a fall in blood pressure.<sup>6</sup>

In addition to the use of various types of parenteral fluid, as discussed above, the treatment of shock involves the administration of oxygen whenever possible,<sup>7, 8</sup> since anoxia is an important cause of capillary damage. Warmth, the Trendelenburg position and morphine are also valuable adjuncts to therapy.

There are a number of ways in which whole blood can be made available in emergencies. In the German army, men are assigned to detachments according to their blood groups, so that if any person in a particular unit needs a transfusion he may receive one from another member of the group. This is scarcely applicable to civilian populations. A second method is the listing of all universal donors,\* who comprise some 45 per cent of the population. These people can then serve as donors in emergencies. If care is taken to eliminate those universal donors who have high titers of isoagglutinins, this is a feasible step, since it is usually those with high titers who cause the trouble that inevitably occurs when universal donors are used indiscriminately.

Witebsky et al<sup>9</sup> have recently shown that it is possible to obtain in pure form the A and B factors that are responsible for the specificity of the red cells of Groups A and B. These are mixed in the proper proportion in sterile ampoules, and the contents of an ampoule, when added to 500 cc. of Group O blood, instantly combine with and neutralize the agglutinins. This blood can then be used indiscriminately without previous cross-

\*Group O by the international nomenclature, Group IV by Most, or Group I by Jansky.

matching Witebsky emphasizes the fact that the blood must be taken from a true universal donor, and suggests that such donors be grouped not only by testing their cells against known serums, but also by testing their serums against known cells. These group factors are nonantigenic, and the subjects do not develop an increased titer of isoagglutinins as a result of the injection of blood neutralized with this material. Witebsky reports quite a large series of successful transfusions of this type. Further experience will be necessary before this type of transfusion can be recommended for any but emergency use. Wiener and his co-workers<sup>10</sup> report a reaction from a second transfusion of Group O blood in a patient of another group. The recipient developed anti O agglutinins as a result of the first transfusion, which reacted with the donor's cells on the second transfusion. Thus, the repeated use of neutralized Group O blood might be dangerous.

It is probable that fresh blood will not be used so much for emergencies as stored blood, since the latter can be kept on hand in adequate amounts and is ready for use at any time. There has been an enormous amount of work on stored blood since the institution of blood banks in many hospitals in this country. The use of cadaver blood has been recommended by certain Russian investigators.<sup>11</sup> It does not require the addition of an anticoagulant, and large amounts of it may be obtained from a single donor. However, when very large amounts of blood are necessary, the difficulties of such collection are too great and its advantages too slight to make it practicable. Placental blood has likewise been used<sup>12, 13</sup> and should provide a valuable supply of blood for the preparation of plasma in general hospitals. It has a low isoagglutinin titer and a low lipid content, giving a very clear plasma.<sup>14</sup> Ham<sup>15</sup> has recently discussed the relative advantages of fresh and stored blood. For the treatment of shock and hemorrhage, stored blood is as effective as fresh blood, and sufficient case reports are now available to show that the incidence of reactions is no greater.<sup>16, 17</sup>

The changes that take place in stored blood have been the subject of exhaustive study by a number of investigators<sup>18-25</sup> whose results are in general agreement. Certain components of the blood deteriorate very rapidly. These are the leukocytes, particularly the granulocytes, which disintegrate within the first two or three days, and the platelets, which likewise disappear very rapidly. The prothrombin and complement titers fall off some-

what more slowly, whereas the red blood cells do not diminish appreciably in number for a much longer period. Since it is the plasma and red blood cells that are important in the treatment of shock, a great deal of attention has been paid to methods of preservation that will prevent the hemolysis of red blood cells. With the ordinary citrate anticoagulant in use in most hospitals, stored blood should not be used after more than ten days, because at the end of this time an appreciable proportion of the red cells have begun to hemolyze. Certain measures are effective in the prevention of hemolysis. The exclusion of air by filling the bottle as full as possible is helpful, particularly when blood is to be transported, since there is less agitation of the red cells under these circumstances. Dilution is also an effective means of diminishing hemolysis, but the addition of glucose is most important. This discovery is not new, but goes back to the work of Rous and Turner<sup>26</sup> in 1916. DeGowin and his co-workers<sup>27</sup> have given a great deal of attention to these problems and use a modification of the Rous-Turner anticoagulant mixture routinely. Five hundred cubic centimeters of blood is drawn into a bottle containing a mixture of 650 cc of 5.4 per cent anhydrous dextrose and 100 cc of 3.2 per cent dihydric sodium citrate in water chilled to  $-5^{\circ}\text{C}$ . The blood is drawn into a bottle of such capacity that, when mixed with the anticoagulant, the container is almost completely filled. Blood taken in this way can be used up to thirty days after bleeding without any increase in the incidence of reactions. DeGowin and Hardin<sup>28</sup> have shipped blood by truck and by plane for many miles in iced containers and have used it after transportation in an attempt to show that this is a practicable procedure for military use. Furthermore, DeGowin and his associates<sup>29</sup> have shown that the incidence of reactions is not increased by administering blood as soon as it is removed from the refrigerator or iced container. DeGowin's recommendations deserve serious consideration, and, where hospital blood banks are in operation, the use of this particular anticoagulant mixture is to be commended, since it will at least double the useful life of stored blood. The drawback is that the blood is diluted, and therefore a larger volume has to be administered with each transfusion, which is a disadvantage when congestive failure or hypertension is present. Also, the increased bulk uses up valuable space in transportation.

Various modifications have been proposed to reduce the dilution factor. Denstedt and his co-workers<sup>30</sup> recommend the following: blood 5 parts, 3.2 per cent sodium citrate 1 part and 5.4 per cent dextrose 1.5 parts. Lewisburg<sup>31</sup> used 300 cc. blood and 150 cc. of an anticoagulant mixture containing 1.05 per cent sodium citrate and 3 per cent dextrose in 0.85 per cent saline solution. Barton<sup>32</sup> takes blood into 2.5 per cent sodium citrate solution and adds 50 cc. of 25 per cent aqueous dextrose solution for every 500 cc. of blood after the blood is drawn.

<sup>11</sup>Witebsky<sup>11</sup> summarizes the published literature on the incidence of Grade III reactions (frank chills) as follows: fresh blood (100 transfusions) 6.0 per cent; stored blood (1973 transfusions) 4.7 per cent.

Considerable attention has been directed to the rise in potassium content of the plasma during the storing of blood.<sup>32-34</sup> This is not the result of hemolysis, since the potassium level rises to a peak of between 60 and 100 mg. per 100 cc. in the first five days of storage, and does not increase so fast thereafter. It probably diffuses from the red cells in addition to being liberated by the disintegrated white cells. Blood with this potassium content has been shown to be innocuous by DeGowin et al.,<sup>35</sup> although some workers have suggested that certain unexplained reactions have arisen from its use. The sodium content of the red cells becomes about four times normal during storage, and this produces an increase in the sodium content of the red blood cells of the recipient after transfusion. However, within twenty-four hours, the sodium content of the recipient's red blood cells returns to normal, indicating the restoration of cell electrolyte balance, once these abnormal cells are put into circulation.<sup>36</sup>

Several groups of workers<sup>36-38</sup> have studied the fate of the red cells of stored blood after transfusion. This is done by various modifications of the technic devised by Ashby. Such studies indicate that the cells of stored blood survive nearly as well as the cells of fresh blood, provided the cells do not show an increase in fragility or the blood an appreciable amount of hemolysis before it is used. Certain cells of stored blood become more fragile on storage, and, once transfused, these cells are hemolyzed in the body of the recipient. Thus with ordinary citrated blood kept longer than seven days,—in which tests show that an increased in vitro fragility is present,—bilirubinemia and jaundice may develop in the recipient during the first twenty-four hours.<sup>37-39</sup> Even under these circumstances, it is pointed out that an appreciable number of the red cells survive and that iron from the hemolyzed cells may be utilized to produce new hemoglobin. Wiener and Schaefer<sup>39</sup> have shown that every day of storage in citrate diminishes by about six days the life of a red cell after transfusion, and that it is therefore bad practice to use blood kept more than ten days with plain sodium citrate solution, or more than thirty days with dextrose-citrate solution. They also claim that dextrose, when added to the anticoagulant, increases the life of the cell after transfusion as well as before.

A final point of significance in the use of stored blood is the necessity for having a filter of some type in the outflow line. Small clots are prone to form in both citrated plasma and blood on storage in the cold, and it is essential to use some

method of removing such clots if reactions are to be avoided. Various types of filters, of wire or gauze mesh, have been devised and are available in most commercial outfits.

Although blood is ideal for the treatment of hemorrhage as suggested above, plasma may be used to restore the blood volume and maintain an effective circulation. In crushing injuries, burns, peritonitis and pulmonary edema from poison gases, shock occurs mainly from the loss of plasma, and plasma is not only satisfactory but far better than blood as a therapeutic agent. Since plasma can be kept much longer than blood and, when pooled, can be used without previous cross-matching, it has come into wide use in emergency therapy. Many papers<sup>40-45</sup> in the literature stress the value of plasma in the treatment of secondary shock, both experimental and clinical. It has been used on a wide scale in England in the treatment of shock and acute hemorrhage, where it has become customary to give 500 to 1000 cc. to a shocked patient, and if further therapy is necessary 500 cc. of blood before administering more plasma.<sup>46\*</sup> The studies of a number of workers, particularly Scudder and his associates,<sup>43</sup> have emphasized the benefit of simple observations such as the hematocrit, hemoglobin and plasma specific gravity values in following shock patients, because they give valuable information *before changes in blood pressure occur*. In air-raid casualty stations, little more is possible than an estimation of the hemoglobin content of the blood and a close watch of the patient's blood pressure. All the English workers have pointed out that blood pressure is a far more reliable guide than pulse rate, and that the effect of the administration of plasma on the hemoglobin content of the blood is a very good index of whether blood as well as plasma is necessary.<sup>40†</sup> If the hemoglobin is lowered well below normal by the administration of a liter of plasma, the patient should receive some whole blood. As pointed out above, when the hemoglobin is already quite low as a result of spontaneous hemodilution, prolonged oozing of blood or previous anemia, the administration of plasma may be harmful.

Pooled plasma can be used in extremely large

\*Some idea of the volumes of blood and blood substitutes necessary for the treatment of severely shocked patients may be obtained from a report of the treatment of an injured flyer of the Royal Air Force, who received 2160 cc. of pooled plasma and 2700 cc. of Group O blood in sixteen hours, with eventual recovery.<sup>47</sup>

†Bushby, Kekwick and Whitby<sup>40</sup> point out that the blood volume, and hence the approximate amount of blood lost (by subtracting the blood volume from the normal estimate of 40 cc. per pound), can be calculated after plasma transfusion by the following formula:

$$\frac{\text{Blood volume (cc.) before plasma}}{\text{Hematocrit or hemoglobin per cent after plasma}} = \frac{\text{Blood volume (cc.) + plasma (cc.) given}}{\text{Hematocrit or hemoglobin per cent before plasma}}$$

doses without cross-matching. Levinson and Cronheim<sup>50</sup> have shown that the isoagglutinins in a particular sample of serum are markedly decreased if it is mixed with several other samples of human serum. These observations have been extended and amplified by British workers,<sup>51</sup> and it is apparent that this suppression of the isoagglutinins results from their neutralization by blood-group substances A and B present in the plasma. The proportion in which plasmas should be pooled depends on their relative agglutinin contents, but a formula that has been used with success in England depends on mixing two parts of Group O plasma with four parts of Group A plasma and one part of Group B plasma. Many workers merely pool eight to ten plasma samples without regard to blood groups.<sup>52</sup> It is possible that a plasma with a very high agglutinin content pooled in this routine fashion might still cause trouble, and if hemolytic reactions occur with pooled plasma, the isoagglutinin content of the pool should be determined.

The use of plasma in the treatment of shock is a vital subject and one in which a great many disputes are going on among workers in the field. The first dispute concerns the method of preservation and preparation of the plasma. If plasma is not separated in the first two days after the blood is drawn, its potassium content will be relatively high. However, there is little evidence that this is particularly harmful. In most blood banks, it is now the custom to separate the plasma after the expiration date of the stored blood, although it doubtless would be ideal to separate the plasma in the first twenty-four hours. A number of methods have been devised for preservation. If plasma is to be preserved in its liquid state, there are two dangers: first, the formation of small clots, which can be taken care of by using a filter in the apparatus for injection, and secondly, bacterial contamination.<sup>53, 54</sup> Experiments by British workers<sup>55</sup> have shown that no antiseptic or bacteriostatic agent is very satisfactory in plasma. Proflavine in a dilution of 1:100,000 is probably the best, but is not effective for more than two or three days. The sulfonamide drugs, although quite effective as bacteriostatic agents in whole blood stored in the cold, are not effective in plasma stored either in the cold or at room temperature. Therefore, very strict asepsis must be maintained in all the processes of collection, pooling and bottling of plasma. If possible, everything should be done with a closed system, and the English have come to the conclusion that if plasma is to be kept in the liquid state for any length of time it must

be passed through a bacteriologic filter to ensure sterility. It is very difficult to filter plasma through a Seitz filter, which is the most convenient type to use, because calcium present in the asbestos filter pads combines with the citrate and clotting occurs. Bushby and his co-workers<sup>56</sup> have devised a method for washing the pad intermittently with a strong citrate solution, so that the plasma may be filtered in reasonable amounts. Thalhimer<sup>57</sup> removes most of the calcium from the pads by soaking them in hydrochloric acid. Another group of workers<sup>54</sup> in England add a solution of calcium chloride to the plasma in a flask containing glass beads. The plasma is then agitated. As clotting occurs, the clot is broken up into small masses by the agitation, and a large yield of serum is obtained. This defibrinated fluid can be filtered readily through a Seitz filter and, although it contains a considerable amount of calcium, has apparently been used without reactions.

Probably the most effective way to preserve plasma is to freeze it.<sup>58</sup> In hospitals, where refrigeration is no problem, this is the ideal method. The plasma may be separated by centrifugation in closed bottles, aspirated aseptically into a pooling bottle, reaspirated into 250-cc. or 500-cc. bottles as pooled plasma, and frozen within a few hours of being drawn. It may be frozen and stored in an ordinary low-temperature mechanical refrigerator used commercially for frosted foods, which maintains a temperature of -10 to -15°C. It can be kept in this manner for very long periods without danger of bacterial contamination, or deterioration of such unstable fractions as prothrombin and complement. When ready for use, it may be rapidly thawed at 37°C. and administered to the patient.

When refrigeration is impossible, dried plasma can be used. Three general methods of drying have been advocated.<sup>59-61</sup> The first, originally designed by Thalhimer<sup>59</sup> for the concentration of convalescent serum, consists in rotating the plasma in cellophane bags in a stream of warm dry air. The water evaporates, until finally the plasma solids are left as a dry powder in the bag. This method, which has been advocated by Hartman<sup>60</sup> and used successfully by him, is valuable because of its cheapness and simplicity. The second method, which makes use of vacuum distillation as the plasma is sprayed into a heated chamber, seems less effective because it requires heating and the transfer of the product from one container to another, with a consequent danger of contamination.<sup>61, 62</sup> The third method of drying de-

depends on evacuation and consequent evaporation of water from the frozen plasma. One process involves the preliminary rapid freezing of the material, which then remains frozen throughout the evacuation process by virtue of the rapid evaporation of water vapor.<sup>63-67</sup> The other type involves freezing as a result of the evaporation itself, which occurs very rapidly as the pressure in the container falls to nearly a complete vacuum.<sup>68-71</sup> There are variations of these methods, involving the type of apparatus used to trap the water coming off the plasma, but the principles involved are much the same. Such plasma desiccated from the frozen state is very little altered, since it is frozen very rapidly and has an extremely low moisture content. In this state, the plasma will keep for years if it is protected from the penetration of water vapor from the atmosphere. To ensure this, the material must be kept in sealed glass ampoules or else in rubber-stoppered bottles inside evacuated or nitrogen-filled containers. It can be reconstituted by the addition of appropriate amounts of sterile distilled water as normal plasma or concentrated plasma of varying strength. Such dried plasma will obviously be extremely useful as a readily available blood substitute for use in out-of-the-way places.

Besides disputes about the method of preparation and preservation of plasma, there is an argument about whether serum or plasma may be used interchangeably, and another about whether concentrated, dilute or isotonic plasma should be used in the treatment of shock. Adequate evidence is not available on either of these points to date. However, incomplete reports indicate that, for some reason as yet not understood, reactions are more frequent with serum than with plasma, whereas reactions are no more frequent with plasma than with blood.<sup>72-74</sup> Those who have had experience with the preparation of serum do not seem to have had many reactions with their own product,<sup>54, 75-78</sup> but serum cannot be recommended for general use until more evidence regarding its innocuousness is at hand. Its main virtue is that it does not clot on passage through a Seitz filter, and hence it is more easily prepared on a large scale.

The dispute concerning the value of concentrated plasma or serum cannot be settled. Hill and his co-workers<sup>79-81</sup> have used four-times concentrated plasma a great deal in the treatment of shock in hospital patients, and their clinical results seem very favorable. In certain English reports, concentrated serum produced reactions, and often thrombosis of the vein, but this product

was concentrated by partial evaporation of the water from the serum, and had not been reconstituted from the dried state. It seems reasonable to expect that concentrated plasma is effective in the treatment of shock when adequate reserves of fluid are present in the tissues. On the other hand, in the presence of dehydration, the administration of a hypertonic solution is obviously contraindicated. More work will need to be done on this phase of the question.

An entirely new approach to therapy with blood plasma has been proposed by Cohn and his associates.<sup>82</sup> Instead of using whole plasma for every condition, he proposes to use fractions of the plasma for specific purposes. In shock, the important point is to restore blood volume. The most useful fraction of blood plasma in maintaining blood volume is albumin, which by virtue of its greater net charge and smaller molecular size, plays a greater role than the globulins in maintaining the normal osmotic relations of the blood and tissue fluids. Serum albumin is not only present in greater amounts than the other serum proteins, but also, because of its physicochemical properties, more stable and more soluble. These properties render it a theoretically ideal substitute for whole plasma in the treatment of shock.

This work has been made possible by the development in Cohn's laboratory of methods of fractionation of the plasma proteins whereby large-scale production is made feasible.<sup>83</sup> This depends on the substitution of alcohol—a cheap, commercial reagent that can be distilled off, condensed and used again—for ammonium sulfate as a precipitant. The precipitation is carried out in cellophane cylinders immersed in mixtures of alcohol and water, in which the concentration, pH and temperature are carefully controlled. The precipitate of albumin obtained can be readily dried, since it carries only a small volume of alcohol and water down with it, both of which are volatile at low pressures. Once dried, the material can be stored without precautions, and can be dissolved in buffered saline to any desired concentration when needed. Twenty-five per cent solutions of human albumin pass readily through a Seitz filter. The ease of sterilization and great solubility of this material make it possible to prepare highly concentrated solutions that take up very little space and are remarkably stable. The compactness and low viscosity of this human albumin preparation make it an exceedingly convenient form of substitute for whole blood, since it does not have to be reconstituted like dried plasma and is considerably less bulky. Clinical trials with



concentrated human albumin are under way, and it may play a very useful role as a therapeutic agent for the treatment of shock in emergencies.

Some of the earliest attempts at blood transfusion were made with heterologous blood, and usually resulted in fatal accidents. However, with the advent of plasma transfusion, interest has been revived in the use of heterologous plasma. Wangensteen and his associates<sup>84</sup> have used bovine plasma as a convenient form of plasma protein for parenteral administration to surgical patients unable to take food by mouth. His experiments have shown that bovine plasma can be administered in large doses to human beings, without fatal reactions. A number of moderate reactions occurred, but he successfully treated one patient in shock from an acute gastrointestinal hemorrhage. In following up Wangensteen's work, bovine plasma has been used as a source of purified albumin.<sup>85</sup> Work with this material is under way at present, but is still in the experimental phase. Immediate reactions are fairly well eliminated by the use of a sufficiently pure bovine albumin instead of whole plasma. The incidence of sensitization to beef products and serum disease with such a highly purified albumin is being carefully investigated.

Keys and his associates<sup>86, 87</sup> have recently noted their interest in this problem. They have separated albumin fractions from the serums of a number of animal species, but apparently have not been able to find any nonantigenic heterologous proteins for use in man.

It is too early to evaluate work of this type, but it represents an important experimental approach to the problem of providing cheap and readily available blood substitutes.

Other solutions have been proposed for the restoration of blood volume. Crystalloid solutions, such as saline, Ringer's solution and glucose, are of course extremely useful adjuncts to therapy, but their effect in shock is transient, because the fluid is not retained in the circulation. A number of workers have explored the possibility of using hemoglobin as a source of protein that would not only act to restore blood volume by virtue of its osmotic pressure, but would also be able to carry oxygen. Amberson<sup>88</sup> has shown that an animal deprived of most of its blood will remain alive for hours if it is infused with a hemoglobin-Ringer's solution. The trouble with hemoglobin as a blood substitute is that, although relatively innocuous, the molecule is treated as a foreign substance and is excreted to a considerable extent through the kidneys, where it may be precipitated as hematin in the tubules when an acid urine

is secreted, with resulting kidney damage. This is thought to be the mechanism of anuria in transfusion reactions.<sup>89-91</sup> A number of workers have recently demonstrated that fairly large amounts of hemoglobin may be given intravenously to human beings without untoward results.<sup>92, 93</sup> If measures to maintain an alkaline urine are adopted, such a hemoglobin-Ringer's solution has interesting possibilities, but it is hard to believe that a substance potentially dangerous in large amounts can replace the other proteins that are retained so much more effectively in the blood stream. Six per cent gum acacia in saline was introduced in World War I as a solution possessing the osmotic and viscous properties of blood.<sup>94</sup> Many of the results in shock were excellent.<sup>95, 96</sup> However, the evidence indicates that the gum is deposited in the liver cells, and the possibility of producing permanent liver damage cannot be dismissed too lightly when it is planned to use very large doses.<sup>88-97</sup> Taylor,<sup>98</sup> in Canada, has devised a solution of fish gelatin or isinglass, which seems to be relatively nonantigenic, and which in acute experiments in dogs was able to restore blood pressure after hemorrhage. Comparative studies<sup>99</sup> of various solutions in the therapy of acute hemorrhage in cats showed that gum acacia, hemoglobin-Ringer's solution, dilute plasma and serum were inferior to isotonic plasma and blood.

Another type of solution that may have properties of considerable value in the postoperative care of wounded patients is casein hydrolysate, which Whipple and his co-workers<sup>100</sup> and others<sup>101, 102</sup> have shown to be an extremely powerful stimulant to plasma-protein production when given intravenously. It should not be employed in the treatment of shock, but may be used in patients unable to take protein food by mouth. It consists of a mixture of amino acids and polypeptides derived from casein by enzymatic digestion.

From the practical standpoint, whole blood is unquestionably the ideal substance for the treatment of acute hemorrhage. Since it is not instantly available for use in the field and cannot be stored without refrigeration, plasma forms a very valuable substitute for immediate therapy, which can later be supplemented by blood transfusion when necessary.\* Human albumin, by virtue of its convenient form, may turn out to play a valuable role in emergency treatment. Plasma and

\*After removal of plasma, the remaining red-cell suspension may be used in the treatment of anemic patients.<sup>103</sup> The amount needed may be calculated from a modification of Marriott and Kelwick's formula<sup>104</sup>:

$$\frac{\text{Per cent rise in hemoglobin desired}}{100} \times \frac{\text{Normal blood volume (cc.)}}{\text{Whole blood (cc.) required}} =$$

albumin are superior to blood in the treatment of burn shock. The use of gum acacia will probably be restricted to nephrotic edema, in which it may be more valuable than any form of plasma protein because it is not excreted in the urine.<sup>105</sup>

## NEW TYPES OF TRAUMATIC INJURIES

### *Blast Injuries*

During World War I, a number of cases were observed in which death occurred without detectable injury. Such deaths from apparent concussion have occurred in the present war among people who were close to the points of explosion of large bombs. A considerable amount of experimental work has been done in England by Zuckerman<sup>106</sup> on the pathogenesis of this type of injury, and it has been found that pulmonary lesions are quite constant. These consist mainly of hemorrhages into the substance of the lung and the alveoli, with some bleb formation under the pleural surfaces, on which scattered petechial hemorrhages may be seen. Blood is usually found in the upper air passages, and x-ray films show various changes, including emphysema, mottled areas and patches of atelectasis. His investigations have shown that these injuries are produced by the pressure wave of the blast and not by the subsequent low pressure, as was first supposed. Covering the animals with a heavy layer of sponge rubber prevented the pulmonary lesions and protected the animals from the effects of the blast.

Two series of human cases have been reported. One group of patients known to be exposed to blasts at close range was studied from eight to ten days after the primary injury, but the findings were somewhat inconclusive.<sup>107</sup> The other group consisted of fatal cases in which post-mortem examination showed changes very similar to those found in the experimental animals.<sup>108</sup> In a few cases, lethal concentrations of carbon monoxide were demonstrated. The significance of this syndrome is that considerable hemorrhage may take place in the lungs without clinical symptoms. Therefore, patients known to have been exposed to blasts at close range should be kept under observation longer than their apparent condition warrants, since the x-ray and pathologic changes are always greatly in excess of the symptoms. The similarity of these cases to what has been referred to as traumatic pneumonia, occasionally observed in civilian practice, is striking. All observers agree that, although the pulmonary lesions may be important, they are not the cause of

death, but merely one manifestation of the injury sustained by the organism.

Another syndrome of great interest, which has been described, so far as I know, for the first time during this war, is uremia complicating crush injuries, particularly of the extremities. A number of cases have been reported in the recent British literature of patients who sustained injuries of moderate or marked severity in which there was crushing of muscle tissue.<sup>109-112</sup> In these patients, after apparent recovery, oliguria developed, then anuria, edema of the crushed limb, azotemia and finally death on the sixth to eighth day after the injury or, in some cases, gradual recovery. The urine in such cases, when any was passed, was positive to benzidine, showed coarse brown granular casts, and was rather dark. Studies of the blood of these patients showed, in addition to a high figure for nonprotein nitrogen and a progressive acidosis, a marked rise in the concentration of serum potassium. The pathogenesis of this type of uremia was not understood at first, but Bywaters and Delory,<sup>113</sup> who described some of the first cases and who have studied the condition intensively, have shown that the pigment excreted in the urine that gives the benzidine reaction is not ordinary hemoglobin, but myohemoglobin. This pigment, of course, is derived from muscle, presumably in the injured area, and the likeliest explanation for the uremia seems to be the precipitation of myohematin in the renal tubules, producing anuria in the same manner as hematin after a hemolytic transfusion reaction. This suggests that the administration of fluids and alkali is advisable as early as possible for patients trapped in such a way that crushing injuries are incurred.

## CONTROL OF AIR-BORNE INFECTIONS

Last year's review<sup>114</sup> mentioned briefly some of the possibilities in the control of air-borne infections, which constitute the most serious menace to health in crowded air-raid shelters. Respiratory diseases are the most difficult of any group of communicable diseases to control, and English and American workers have been studying this problem intensively in the past year. Their findings may prove of great value in the large military camps of the United States.

A recent report by Andrewes<sup>115</sup> summarizes his work and that of his colleagues. It points out that air-borne infection travels in three ways. The first is by coarse droplets, which are projected into the atmosphere by sneezing and coughing and

fall to the floor in a short time because of their size. Control of this form of spread is possible by adequate screening of individual patients and by proper masks, the most effective one that the English have found being made of a sheet of cellophane, which is impermeable to bacteria and viruses. It is worth pointing out that in the Boston Lying-in Hospital a mask consisting of a layer of nonabsorbent cotton folded into a layer of gauze has been used for some time. This utilizes the principle that bacteriologists have used for many years to exclude bacteria of the air from their cultures, and is highly effective. Since such a mask is cheap and can be discarded after use, it should replace the ordinary gauze mask used by most hospitals.

The second form of air-borne infection is by droplet nuclei. These are minute droplets, so small that they remain in suspension in the air for long periods. Each droplet nucleus may contain a few bacteria, and it is in this form that infection is borne about in the air through buildings, as has been demonstrated most clearly by the work of Wells and Wells.<sup>110</sup> Possibly, this type of infection can be controlled by the use of ultraviolet light. The English workers suggest that the air in shelters be drawn through a heavy muslin screen, which will serve as a filter for large droplets, then through a tunnel, in which ultraviolet lights are placed, and then ejected as sterile air into the room again. This is more effective and less expensive than placing ultraviolet lights about a room, as has been done in operating amphitheatres. Another method of combating droplet nuclei is by the use of aerosols. This development is due mainly to the studies of Trillat<sup>117</sup> and Twort et al.<sup>118</sup> Aerosols are antiseptic liquids nebulized in such a way as to form minute droplets much like the droplet nuclei mentioned above. These then remain suspended in the air for long periods as a fine mist, which is unnoticed by anyone present in the room. By such fine dispersion, a small amount of the liquid will fill quite a large room, and yet in each individual droplet the antiseptic solution can be kept at an effective level. Droplet nuclei and bacteria are attracted to the aerosol droplets, and the bacteria are killed by the antiseptics present in them. Hexylresorcinol in propylene glycol is the most effective known aerosol, but sodium hypochlorite can be used in 0.5 per cent solution very effectively without irritation to the mucous membranes. The British are experimenting with the use of these aerosols in the sterilization of shelters immediately before and after their occupation.

The third way in which bacteria are carried in the air is by dust. Droplets fall to the floor, the water evaporates, and the bacteria, particularly hemolytic streptococci and diphtheria and tubercle bacilli, may remain viable for long periods, to be swept up in the air with any disturbance. In this form, the organisms are resistant to ultraviolet light. Likewise, they are present on blankets, and it has been shown that the bacterial count of the air rises following bed-making in a hospital ward. To control this type of infection, the British workers have found the application of oil to be most effective. Mineral oil is rubbed on the floors, and although a certain amount of luster is lost, sweeping of floors so treated will not throw bacteria up in the air. Hospital blankets can be treated in such a way with mineral oil in naphthalene or some similar solvent that the blankets appear perfectly normal. However, they retain about 3 per cent by weight of oil, and this suffices to trap bacteria.

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This brief report on progress in military medicine shows that the necessities of war have served as a stimulus to research that may have a vital bearing on medical practice and the prevention of sickness in peace as well as in war.

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We are not told on physical examination whether he did or did not have any tophi. Regardless of this fact, I think the diagnosis of gout is the most likely one. The patient had recurrent attacks in one or another of the big toes, presumably in the metatarsophalangeal joint. It is interesting that, as the swelling of the feet subsided, the gout became more noticeable; this is proof of the well-known fact that an attack of gout can be provoked by induced or spontaneous diuresis. It is extremely unlikely that the joint disturbances could be due to infectious or rheumatoid arthritis, which, over a period of years, would most certainly have resulted in joint disability between attacks. The entire clinical picture during the five months previous to entry is perfectly compatible with gout.

It is interesting that the patient was pale and slightly short of breath, with blood in his nose, and some explanation of that should be made. The urine showed a ++++ test for albumin. The urine concentration test showed a specific gravity of 1.011, and a phenolsulfonephthalein test showed no excretion of the dye in two hours. That is the first definite clue that there was something very wrong with the kidneys. The blood picture showed a moderate normochromic anemia. So far as the diagnosis of gout goes, the uric acid level of 10.3 mg. per 100 cc. is of no help, because it is elevated in every case of renal insufficiency with marked nitrogenous retention. Is the uric acid more elevated in relation to the non-protein nitrogen in the presence of both gout and uremia? I do not know, but I think so. The formol-gel test is positive in most cases of cirrhosis of the liver. I am a little disturbed that the liver function, as measured by dye excretion, was so good, and that the serum van den Bergh was normal. I should expect, in a typical case of portal cirrhosis, a slight degree of dye retention. Nevertheless, that does not mitigate against the diagnosis of portal decompensation. Of course, in any person with cirrhosis of the liver who vomits or passes blood, our first thought concerns varices in the esophagus. On the other hand, the fact that the x-ray film did not show them does not rule them out. We know that in alcoholism there are other causes for vomiting; one that might result in a severe hemorrhage and still not be seen by x-ray is severe gastritis. So far, we have no evidence for or against that diagnosis.

X-ray examination showed a fair degree of narrowing of the joint spaces in the feet, with a certain amount of atrophy. The hands showed little except degenerative changes. In other words,

the x-ray picture was compatible with a diagnosis of gout, that is, it showed very little bone or joint change. On the other hand, even if the findings were more marked than these and even if they simulated rheumatoid arthritis more seriously, they would be compatible with gout, as we have seen in quite a few cases in this hospital.

The electrocardiogram was not significantly abnormal.

According to the record, the cervical spine was involved. That is disturbing, if true, because by and large it is extremely rare for acute gout to involve any part of the cervical, dorsal or lumbar spine. I rather imagine that this probably represents acute tenosynovitis in the ligaments or tendons of the neck.

There was a very marked degree of hypocalcemia, high phosphorus retention due to kidney insufficiency, and marked acidosis, with only 50 per cent of the normal carbon dioxide combining power. One would certainly expect a patient with a calcium of 6.3 mg. per 100 cc. to have a positive Chvostek's sign. I rather imagine that this patient did not have it because of the high degree of acidosis.

The sodium citrate and aluminum hydroxide were given presumably to try to normalize the calcium-phosphorus metabolism; however, eight days later it was about the same. We are not told whether the patient received specific therapy for the gout, such as colchicine.

We are now faced with the terminal event, and we are unable to obtain further information about the fundamental diagnosis. In a person of sixty-two with hypertension and gout, I should say the most likely thing would be a severe degree of nephrosclerosis, a terminal vascular disease in the kidneys. There is nothing in the past history to suggest acute or subacute glomerulonephritis, any infectious type of nephritis, pyelonephritis or any other type of renal disease. I say "with gout" because renal vascular disease is commoner in people with long-standing gout than in other people.

Is this a gouty nephritis? I think it has been decided that we do not know exactly what gouty nephritis is. True, some people at autopsy show high degrees of vascular change and some uric acid crystals in or around the tubules. I should say that if this attack was acute it was not due to a primary type of renal disease.

In the record of the last admission, there is a definite change in electrocardiographic findings from what was previously recorded—a low T<sub>1</sub> five days after acute chest pain. Five days later, T<sub>1</sub> was diphasic. In view of the history, the

electrocardiographic findings, the clinical findings and the acute cardiac decompensation, there can be little doubt that there was coronary occlusion, with an infarct of the anterior type. We are not told very much at the time of the last admission about the amount of fluid in the abdomen or the feel of the liver after paracentesis. There is no question that the terminal event was coronary occlusion and cardiac failure.

He also had blood in the stools as a terminal event. Whether that was bleeding from esophageal varices or gastritis or possibly from the hiatus hernia, which is rather unlikely, or a uremic colitis, it is impossible to say.

I have mentioned most of the differential diagnoses, and I sum up the list of probable diagnoses as follows: gout, portal cirrhosis, arteriosclerosis, hypertension, nephrosclerosis with uremia, coronary occlusion with cardiac failure, and questionable gastritis or esophageal varices as the cause of the bleeding. I should like to add that I am still disturbed by the fact that the liver is reported to have felt smooth and round. I do not recall ever having seen a case of portal cirrhosis in which the liver felt smooth.

DR ALFRED KRANES: Do you not think that, clinically, the liver is always smooth in portal cirrhosis?

DR JACOBSON: I think it is irregular. DR KRANES: Do you think one can always feel the small nodes clinically?

DR JACOBSON: No, I mean after paracentesis, when the abdomen is flat.

DR TRACY B. MALLORY: I should be inclined to agree with Dr. Kranes. I am skeptical if anyone feels irregularities in a cirrhotic liver. At the stage when the liver is big enough to be felt, the granules that are present are particularly small, and it seems to me that it would be impossible to feel them.

#### CLINICAL DIAGNOSES

Gout  
Chronic glomerulonephritis  
Uremia  
Cirrhosis of liver

#### DR JACOBSON'S DIAGNOSES

Portal cirrhosis  
Hypertension  
Generalized arteriosclerosis  
Nephrosclerosis  
Uremia  
Gout  
Coronary occlusion  
Cardiac failure  
Gastritis (?) or esophageal varices (?)

#### ANATOMICAL DIAGNOSES

Gout  
Alcoholic cirrhosis of the liver  
Splenomegaly  
Esophageal varices  
Chronic vascular nephritis  
Uremic colitis  
Hypertrophy of the heart  
Bronchopneumonia

#### PATHOLOGICAL DISCUSSION

DR MALLORY: At the post mortem examination, no tophi were discovered. Many of the joints showed extensive urate deposits. About 5 liters of ascitic fluid was found.

The liver was larger than normal, and possibly a reason for the smoothness was the fact that it was rather markedly frosted with a heavy layer of white fibrous tissue, so that even a 1 cm. nodule certainly could not have been felt. The cut surface of the liver showed a marked increase in fibrous tissue, complete destruction of the architecture and innumerable little granules of encapsulated liver tissue, the largest of them was 3 mm. in diameter, however, and the vast majority were 1 or 2 mm. Microscopically, it was typical of an alcoholic cirrhosis. The spleen was somewhat enlarged, weighing 350 gm., and also showed a frosted capsule. The esophagus showed very evident varices. It is surprising that they were not shown by the x-ray studies, which often show varices that we have difficulty in finding at autopsy. None of them, so far as we could make out, had bled recently. At any rate, there was no ruptured varix at the time of death. There was no marked grade of gastritis, but the colon showed a very severe hemorrhagic colitis and was filled with a bloody mucous fluid. I think the terminal hemorrhage from the bowel almost certainly came from the colon rather than the esophagus. Some of the earlier episodes of hematemesis probably did come from the esophagus. The colitis was not specific in character and corresponded to what we usually call "uremic colitis."

The heart was hypertrophied, but we could find no infarct, and the coronary arteries were very good, not even markedly narrowed, there was no pericarditis. The lungs were normal.

The kidneys were small, the pair weighing 220 gm. The gross appearance was that of nephrosclerosis. Just after the autopsy, some pieces of kidney were examined under the dissecting microscope, and it was thought that some uric acid crystals could be identified at the time. Later, sections of alcohol fixed material stained specifically for uric acid failed to show it, so that I think

so caused the mild but definite polycythemia, more cells being needed to carry the same amount of oxygen from the limited lung surfaces. It is amazing that the tumor grew to this size and failed to cause urinary changes.

#### CLINICAL DIAGNOSIS

Hypernephroma, with widespread metastases.

#### DR. CHAPMAN'S DIAGNOSES

Portal cirrhosis, moderate.

Multiple lipomas.

Hypernephroma, left kidney, with widespread metastases.

Polycythemia, secondary to obliteration of the lung fields.

#### ANATOMICAL DIAGNOSES

Portal cirrhosis of the liver.

Hepatoma, with metastases to lungs, bone and left adrenal gland.

Tumor thrombi of hepatic vein and inferior vena cava.

Splenomegaly, secondary to portal obstruction.

? Polycythemia vera.

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This was obviously a very puzzling case from the diagnostic point of view. There were many leads, but each of them seemed to be contradicted by some other finding, or to be absolutely without confirmatory support. It is extraordinary, for example, to find a man dying of metastatic malignant disease with a polycythemia instead of an anemia. The Pancoast syndrome suggested a primary bronchiogenic carcinoma, but the x-ray examination showed clearly that the tumor was outside the lungs. The pyelogram suggested hypernephroma, but the urine was normal and the history of alcoholism and the suspicious evidences of cirrhosis seemed simply a complicating factor. The clinicians on the wards reasoned essentially as Dr. Chapman did, and likewise came to the conclusion that hypernephroma was the best bet. As a matter of fact, the most important lead in the record was the history of chronic alcoholism, for the patient had a cirrhosis and he had that by no means uncommon complication of cirrhosis, a primary liver-cell carcinoma or hepatoma. The roentgenologist was correct in his opinion that the right lobe of the liver was smaller than normal, but the left lobe was more

than correspondingly enlarged and almost completely replaced with tumor. As these hepatomas characteristically do, the tumor had invaded and grown along the hepatic vein up to the vena cava, into which a nubbin of tumor thrombus that narrowed it by a quarter of its cross-sectional area had projected.

It had metastasized extensively, and there were numerous small tumor nodules in the lungs. The tumor responsible for the Horner's syndrome was metastasis to the seventh cervical vertebra, which had grown forward and downward to displace the apex of the lung. It did not invade the brachial plexus and must have produced its effect by pressure only. Another large metastasis had completely replaced the left adrenal gland, and it must have been adhesions from this tumor mass that were responsible for the deformity of the left renal pelvis. The epigastric mass was, I imagine, mostly the left lobe of the liver, although it is possible that the adrenal tumor may also have been felt. The spleen was greatly enlarged, weighing 800 gm., but they apparently were able to dissociate this from the epigastric mass.

I am entirely at a loss to explain the polycythemia. It was certainly greater than could be explained merely by dehydration. The bone marrow showed, besides the major metastatic lesions, recognized by the roentgenologist, multiple milium metastases, and therefore one would have expected an anemia. The portion not involved by tumor showed an extreme grade of erythrocytic hyperplasia, and was consistent with but hardly diagnostic of a polycythemia vera. I had hoped that the spleen might help us make such a diagnosis, but it showed only the marked sinusoidal engorgement and the fibrosis of the pulp characteristic of long-standing portal congestion, such as is seen with cirrhosis of the liver and in the so-called "Banti's syndrome." Dr. Chapman's suggestion of a secondary polycythemia based on pulmonary insufficiency is interesting, but I am unable to agree with him. The extent of metastatic involvement of the lungs was not nearly so great as we frequently see, and I cannot remember ever to have seen a secondary functional polycythemia based on neoplastic replacement of pulmonary tissue.

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## POSTGRADUATE MEDICAL EDUCATION

THE 1940 report of the Commission on Graduate Medical Education\* devoted more of its space to the discussion of internships, residencies and specialties than it did to the needs of the practicing physician. The commission is aware of the serious problems involved in this wider field, however, for it acknowledged the need of postgraduate education for family doctors from many points of view. The report stated, "The time is now ripe for the development of broad standards of educational content of postgraduate work, standards that will emphasize objectives and stimulate higher achievement without inhibiting widespread

experimentation with means and methods." Particular attention should therefore be paid to an article appearing in this issue of the *Journal*. If the time is ripe, it appears that the program of Tufts College Medical School for postgraduate medical education offers some of the "means and methods."

Three years of experimentation in this field are worth recording. How much of the present program will be continued and how much will need to be readapted, it is impossible to say. The program as a whole has behind it a broad conception of the problem. It visualizes a medical service that is not rendered by the physician alone, but by a group of people and facilities under the direction of the physician. If the physician wants an electrocardiogram, he must have the facilities for obtaining it, and if he cannot fully understand its implications, he must have help in its interpretation. If he is taught what the clinical laboratory can do for him today, a laboratory and a technician must be made available. If he understands and appreciates the possibilities of modern x-ray technic, proper apparatus must be provided. Much of the discouragement of the alert practicing physician comes from his inability to make his own diagnostic knowledge effective through lack of personnel or material, or both. An initial attempt to supply these deficiencies by paralleling postgraduate education with an affiliated system of regional and community hospitals, including all the usual ancillary activities and services, has been made, apparently with a considerable measure of success. The Bingham Associates Fund appears to have made an auspicious entrance into the field of medical education at Tufts.

## THE TREATMENT OF TRAUMATIC SHOCK

ALTHOUGH the problem of shock has continued to challenge investigators since World War I, the present war has given a great impetus to research in this field. Since shock is a state that is difficult to define, and can come about in a number of ways, it is small wonder that the prob-

\*Commission on Graduate Medical Education. *Graduate Medical Education*. 364 pp. Chicago: University of Chicago Press, 1940. P. 200.

TABOR—EDWARD O. TABOR, M.D., of Lowell, died August 25. He was in his sixty-sixth year.

Born in Hanover, New Hampshire, Dr. Tabor received his degree from Dartmouth Medical School in 1901. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow and a son survive him.

## CORRESPONDENCE

### "ACCOUCHEMENTS FOR AMERICA"

To the Editor: Probably doctors know more about economics, politics and other nonmedical subjects than any other group of people, but I humbly beg to differ with the opinion of Dr. Francis H. Higgins on "bargains in babies," which appeared in the August 14 issue of the *Journal*. Our crackpot friends, Herr Hitler and Il Duce, have had similar ideas, but it is emphatically not what we need in this country.

Here is how the scheme would work out: the many intelligent, hard-working and patriotic young couples of the lower middle class would still have only one or two children; they would not feel that they could afford to take advantage of the bargain rates, because they do not have large enough incomes to provide for clothing, food and education for more children. But the people who do not know enough or care enough to limit the number of their children would be encouraged to have even more, if possible, because of the 25 per cent reduction for each succeeding baby. The final result would be an increase in the population, but with an increase in the proportion of those who are relatively unproductive and a corresponding decrease of able professional and technical people. Such a public would eventually welcome a totalitarian government, which would involve, among less important things, regimentation of the medical profession.

Why not put the medical economists to work figuring out some sort of subsidy or bargain rate for the many couples who would like to have more children and who would have more if they felt that they could provide decent living conditions for them? That would be a definitely patriotic step.

C. S. GREENWOOD

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## BOOK REVIEWS

*A Surgeon's Life: The autobiography of J. M. T. Finney.* 8°, cloth, 396 pp. New York: G. P. Putnam's Sons, 1940. \$3.50.

Finney, in his autobiography, covers an interesting period in the development of medicine in America. Trained in the best traditions of his time, at the Harvard Medical School and the Massachusetts General Hospital, he went to the Johns Hopkins Hospital when Welch, Osler, Halsted and Kelly were at their height. The seeds sown by these great pioneers had grown to fruit, and Finney, with his colleagues of the eighteen nineties, reaped a rich harvest. Little was added by the second generation, for it was a time of putting into practice the stimulation received from others, not for the development of new ideas. Many of Finney's contemporaries became good surgeons and fine physicians, but none, save Harvey Cushing, were of the genius type of their predecessors. This, in no way, detracts from the excellent work of Finney and his associates, for they did the best surgery in America of their day, and practiced the best medicine. Finney gives an intimate picture of life at Hopkins, but much of the pic-

ture lacks color and shading. The outlines are discernible, but no clear memory remains after reading chapters, for the whole book lacks body and depth. A few stories help to enliven the drab narrative, and Finney's humor and infectious laughter are felt throughout. He always added a story to any group, and was often called on to relieve tense situations in hospital and overseas during World War I. He was the embodiment of sound common sense, the conciliator and the man of sound judgment. One would choose him, however, rather as a surgeon than as an author, and that is a choice, no doubt, that Finney would agree was the most fitting.

*Diseases of the Digestive System.* Edited by Sidney Portis, B.S., M.D. 8°, cloth, 952 pp., with 176 illustrations and 37 tables. Philadelphia: Lea and Febiger, 1940. \$10.00.

This volume should prove to be an extremely useful text and reference book, for it has been carefully compiled by leading authorities. It presents a comprehensive up-to-date study of gastroenterology. The material is arranged in five parts, as follows: "Introduction," with chapters on history, anatomy, physiology and the interpretation of pain in the gastrointestinal tract; "Etiologic Factors," including parasites, neurogenic factors, gastrointestinal manifestations of other diseases, anemias of gastrointestinal origin, tuberculosis, allergy and the relation of the teeth and diet to gastrointestinal diseases; "Diseases of the Esophagus, Stomach and Duodenum," with chapters on the esophagus, gastritis, peptic ulcer, achylia, cancer, benign tumors, syphilis, linitis plastica, duodenal ileus; "Other Diseases of the Digestive System," including affections of the liver, gall bladder, pancreas and small intestine, and regional ileitis and appendicitis; and "Diseases of the Large Bowel and Rectum," including chapters on functional disturbances, protozoal infections, bacillary dysentery, ulcerative colitis, mucous colitis, cancer, diverticulitis, melanosis, hemorrhoids and lymphatic venereal disease.

The reviewer finds little to criticize. Modern methods of study, including gastroscopy and liver-function tests, receive a fair share of attention. Treatment is well considered in each chapter. Numerous references are given. Illustrations, tables and diagrams are very satisfactory. This book is highly recommended.

## NOTICES

### SEVENTH POSTGRADUATE SEMINAR IN NEUROPSYCHIATRY

The Metropolitan State Hospital, Waltham, recently announced the opening of the Seventh Postgraduate Seminar in Neuropsychiatry.

The course consists of three units: military neuropsychiatry, October 3 to 31; general psychiatry, November 3 to December 12; and general neurology, January 3 to April 10. It is open to a limited number of graduate physicians. The teaching staff comprises a number of recognized specialists in this field throughout the state and is under the direction of Dr. Roy D. Halloran, superintendent, Metropolitan State Hospital, and Dr. Paul Yakovlev, clinical director, Walter E. Fernald State School.

### FORUM ON ALLERGY

The fourth annual Forum on Allergy will be held in Detroit, Michigan, on January 10 and 11, 1942.

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## THE MOSAIC OF ANDROGYN\*<sup>†</sup>

Maleness Within the Female and Femaleness Within the Male

GEORGE DRAPER, M.D.<sup>†</sup>

NEW YORK CITY

LIKE other bisexual forms, the human species is divided into males and females according to the presence of testes or ovaries, with their accompanying external genitalia. Reproduction is the primary purpose of these opposed organ assemblages. But, in addition to the specific function of race perpetuation, each man and woman must likewise serve the law of self-preservation. This vital individual task, among primitive peoples at least, calls for different kinds of qualities that are adapted to the special relation maintained by each sex toward environment.

So far as one knows, the actual phenomenon of reproduction is achieved through the genital organs alone. A person's other task of survival depends on adequate adjustment with a complex environment, which includes human relations. The impulse to survive is expressed extragenitally by the man in manly fashion, and by the woman in womanly ways. The opposite and special endowments for these purposes are in general well known, and are displayed by differences between man and woman in morphology, physiology, immunity and psychology—or as somatic cellular sex in the total organism. This composite structure of masculine and feminine characters has been called "the mosaic of androgyny" ( $\alpha\mu\beta\iota\sigma$  = male;  $\gamma\omega\gamma$  = female). The term is used because the nongenital qualities appropriate to each sex are never complete in a given man or woman to the exclusion of some evidence of the counterpart. Thus, traits that are ordinarily judged to be the man's may appear in the woman to form kaleidoscopic patterns with her own; the reverse is like-

wise true. The contrasting qualities have to do not only with outward design, structure and function, but even more significantly with the extragenital dynamics of the whole person. So far as the relation of human constitution to disease is concerned, the androgynous phase of sex seems to be of greater significance than the genital. And it is for this reason that the terms "andric" and "gynic" (adjectives formed from the joint word's component parts) have been chosen to designate the divergent organismal aspects of man and woman.

Within certain limits, the expressions of cellular sex in adults are modifiable by castration or its milder physiologic analogue,—the climacteric,—or by tumors of various endocrine glands. A good example of this is the greatly increased emphasis on andric characters in patients with adrenal tumors, as described by Gallais.<sup>1</sup> But even in his Case 3, the late effects of the tumor could not have been related to the existing broad shoulders and narrow hips. These andric characters must have been laid down in the genetic plan, or effected at an early embryonal stage by some intrauterine accident. It goes without saying that sex hormones exert a powerful influence on the entire organism. But the effects of castration, for example, are more extensive in the male. Furthermore, the castrated male tends to take on characters that in many respects are similar to the female. This "toward-female" capacity, however, is more marked in some castrates than in others. Among insects it is known that the various somatic insignia of maleness or femaleness may have no relation to the nature of the gonad. From all these observations it seems that sex is something more than the mere presence of a gonad. As Lillie<sup>2</sup> believes, sex is not "an irreversible predestination, but a quantitative over-

\*From the Department of Medicine, Columbia University College of Physicians and Surgeons, and the Presbyterian Hospital. This work was aided by a grant from the Rockefeller Foundation.

<sup>†</sup>Associate professor of clinical medicine, Columbia University College of Physicians and Surgeons, associate attending physician, Presbyterian Hospital.

balance in the direction of one sex or the other."

Andric and gynec characters strongly and subtly woven into the fabric of each one's personality are not unappreciated by laymen. Posture, gesture, voice and the flavoring of individual identities have long been observed and used as a means of classifying people in masculine or feminine categories. Moreover, from groups and audiences composed either of men or of women, the unerring impact of this bisexual otherness can easily be felt. But the awareness of it is more sharply focused in the impression made by a single person. One is quick to recognize the presence in a member of one sex of qualities properly allocated to the other.

To illustrate the divergence of andric and gynec impacts that radiate from groups, an excellent opportunity is afforded by a visit to a large medical clinic. Anyone who has worked long in hospitals has, no doubt, noticed the subtly different atmosphere that one senses in the men's and women's wards. There is an air of tranquillity in the latter. Neatness, decorum and patience fill the place. In some strange manner, women seem more at home there, more appropriate to bed in daytime than men. As one enters the quiet ward, one notices that all the patients seem to be reclining easily in their beds—they are mostly supine, with arms and hands crossed on the midriff or stretched resignedly beside the body. All are relaxed among their pillows. When they turn their eyes and heads to view one's approach, the expressions are not overcurious, and the motions of those who do move are unhurried and deliberate. Then, as one scans the group of patients, one's attention is sharply arrested by the woman in the third bed to the left. She is a vigorous-looking person of about fifty. A shock of white hair, cut short behind and at the sides, surmounts the powerfully modeled forehead and heavy dark eyebrows. Almost imperiously, the restless eyes observe what is going on, and the vigorous mouth and lower jaw are energetically engaged alternately in chewing gum, making thorny remarks and offering innumerable suggestions. The entire personality exudes a force that cuts sharply across the ward's passive atmosphere. The andric qualities of this person, expressed in the masculine modeling of the head, the vigorous gestures and the projection of total organismal energy, are easy to observe.

And when one enters the male ward, greater activity is at once apparent. Things are not so neat and particular as in the women's ward. Some patients are lying with knees up, others are on their sides supporting themselves by one elbow,

still others, with hands clasped behind their heads and elbows wide, are uncomfortably propped by their pillows. Occasionally, one man calls across to a friend in another bed, a radio is switched on, a patient turns awkwardly to see what an intern is doing to his neighbor. Costly of outgoing energy are all these attitudes, which accomplish little. Possibly, they express the need for satisfaction in motion, a response to the man's biologic urge to project his life force on the universe in an effort to arrive at some self-appointed goal.

Sitting at the ward's center table are three patients. Two are playing pinochle and slapping the cards down with gusto. The third attracts attention by the contrast of his attitude and appearance. This patient is an average-sized man, with large hands out of proportion to the limited thickness of his frame, and with a large pale face marked by small features. He sits quietly, hands clasped in his lap and watches the game with a tolerant and gentle smile. Often, he wags his head in mild rebuke, as though to say, "Now, children, not too roughly." When one asks him his occupation, he replies in a high-pitched husky voice with neat diction, "I'm a blacksmith, Sir." A more careful inspection reveals a paradox between this man's trade and total personality. Instead of knotty muscle, his arms and back display a smooth panniculus. Rounded shoulders, slightly prominent belly and mons veneris above curving hips and thighs bespeak a strongly feminine morphology. He patiently waits for his discharge, watches but never joins the ward activities, and creates no trouble for anyone.

From the foregoing description of differences between the impact of the andric or gynec thing that emerges from massed men or massed women, it is possible to recognize that energy, common to both groups, is utilized in quite different ways. It is not the varying magnitude of energy capacity that is the significant difference between the two phases of the androgyny. In many cases, women may be actually stronger than men. But the feminine pattern of energy utilization is fundamentally different from that of the man. The former tends to conserve and build up energy stores and to spend it cautiously. The latter, on the other hand, is prodigal of his virile forces.

The concept of the andric and gynec differences in energy utilization is not new to biologists. Thus Doncaster<sup>3</sup> reflects it in the statement that the egg is large, quiescent and stores up energy. Sperm, on the other hand is small, actively motile and spends energy. It will be noted that these basic differences in the two opposing initial cells are

characteristic of the average adult male and female in practically all species. In the matter of conduct, for example, everyone is familiar—especially the woman—with man's strenuous pursuit of his objective. Once his interest becomes fixed on his heart's or mind's desire, nothing else matters but its achievement. He moves vigorously toward it, overcoming obstacles at any cost, leaving a trail of wreckage behind. The woman, on the other hand, as man well knows, tends to be static. She is not easily mobilized, and therefore often keeps him waiting. Woman must preserve a safer and more stable situation for the security of the offspring and herself. She not only conserves her own strength but reaches out her hand to stay the man's impetuosity, to retain his energy for the supply and defense of her protectorate. Geddes and Thompson<sup>4</sup> have expressed the same thought by saying that femaleness is correlated with preponderant anabolism, maleness with emphatic catabolism.

This view is supported by Riddle's<sup>5</sup> observations on differential basal metabolic rates between males and females. He found that rates for males were consistently higher than those for the opposite sex. If, then, one accepts the notion that in the extragenital phase of human beings the androgynous differences between man and woman are to be found in their types of body form, their conduct and their mental attitudes, one can proceed to a more detailed consideration of individuals of each sex.

#### ANDRIC AND GYNIC QUALITIES

##### Morphology

Viewed from in front or from behind, the basic silhouettes of the male and female forms can be respectively described as one of angular rectilinear-ity or of curving ovoid. The lateral aspect of the woman presents perhaps less of the ovoid outline, but a greater emphasis on localized curving convexities. From in front, the man's arms appear to be hanging freely dependent from the shoulder points, and at the elbow there is little or no obtuse angle known as the carrying angle. His pelvic breadth is notably narrower than that of the square shoulders, and the lower extremities are straight or slightly bowed at the knee. When the heels are approximated the space between the lower extremities presents a characteristic outline (Fig 1). The inner belly of the gastrocnemius is more prominent than the outer, and the outer curve of the calf bends sharply in toward the external malleolus. In the woman, on the other hand, the shoulders are more sloping, and the upper extremity instead of hanging from the acromion point seems to extend the downward mov-

ing neck shoulder modeling in a continuous curving line. The carrying angle is well marked, so that the forearm and hand clear the prominent outward curve of the hip and thigh, which in turn springs from well above the iliac crest. The far wider hip line is determined in part by the bony structure and in part by the greater distribution of fat over the lower abdominal, pelvic and upper thigh areas. The lower extremities are rounded, and when the heels are together, the thighs are approximated from the crotch to the knees, which are pressed in close apposition. Be-

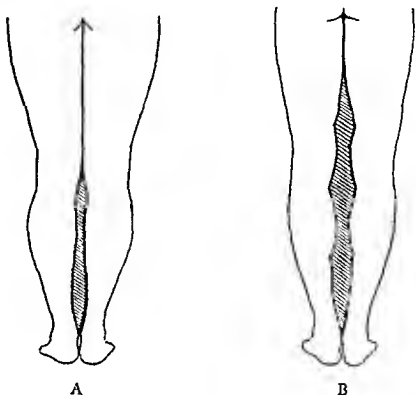


FIGURE 1 Showing Interspace of the Approximated Lower Extremities in Women (A) and in Men (B)

tween the knee and ankle a space appears, owing partly to the genu valgum and partly to the less emphatic inner belly of the gastrocnemius. The outer line of the leg sweeps in an even, continuous curve from knee to outer malleolus.

Besides these more general contours or silhouette contrasts (Figs 2 and 3), differences of surface modeling between man and woman are well known. In men such observable localized bosses or protuberances as may appear are chiefly due to the well developed muscles, which are covered only by a thin layer of subcutaneous fat. What have been ordinarily designated as secondary sex characters, namely, breasts, mons veneris, girdle and thigh fat deposits, on the other hand, constitute the otherness of a woman's surface modeling. The woman's muscles are not large and knotty, and may be completely hidden beneath a fairly thick, smooth panniculus. The distribution and quantity of facial and body hair constitute another well known set of morphologic criteria that differ between men and women.

### Physiologic Panel

Some physiologic phenomena show andric and gynec differences. Perhaps the most notable of these is the basal metabolic rate, which, as mentioned above, is known to be higher for males than for females. It is also usually accepted that red-cell counts and hemoglobin levels are lower for women than for men. Of this, Riddle<sup>5</sup> states: "... present knowledge establishes the probability

and females can be lowered by prolonged inactivity of the animals, as shown by Lusk and DuBois,<sup>6</sup> but such effects of rest are more striking in the male. As Riddle<sup>5</sup> says, "Any sex changes which may occur as a direct result of prolonged inactivity should be in a male-to-female direction." Child<sup>7</sup> believes that differences in susceptibility to external toxic agents are characteristic features of different levels of physiologic gradients, or

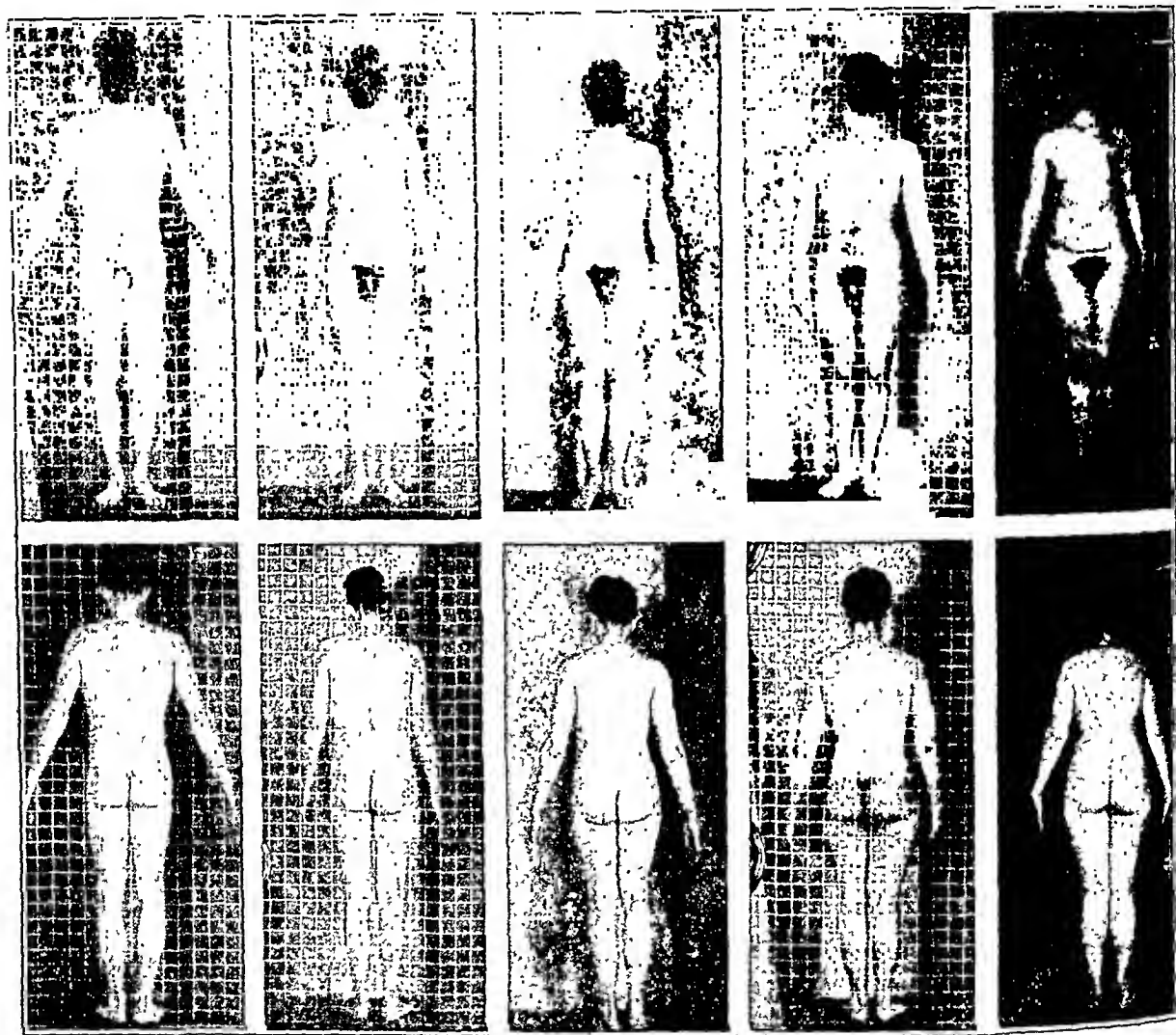


FIGURE 2. Showing Increasing Emphasis on the Gynec Factor in the Male Morphology.

that these excess values [that is, red-cell and hemoglobin] in males cling to maleness because they are a real part of the metabolism machine and because sex difference takes its basis and origin in metabolic difference." Here the oxygen-carrying capacity seems to indicate a connection with the metabolic level, and the pulse rate has usually been said to be higher for women than for men. The notion that metabolic rate and sex difference are closely related has been noted by numerous observers. Furthermore, the rate in both males

more specifically that a relation exists between susceptibility and basic metabolic rate:

With certain qualifications and limitations, it appears to be true that the rate of oxidation is in some degree a measure of the rate of living. It has also been shown that in the less highly specialized protoplasm susceptibility to certain ranges of concentration or intensity of external agents is an indicator of rate of oxidation and may be used as a rough comparative measure of differences in rate. There is, therefore, a real experimental basis for the statement that susceptibility is in general a measure of rate of metabolism or more particularly oxidation.

Thus, all the observations and experiments related to metabolism and sex difference support the notions of the biologists, Doncaster<sup>3</sup> and Geddes and Thompson,<sup>4</sup> that gynec values relate to ques-

findings are interesting and show for example the following generalizations.

Masculinity in men at either of two educational levels is associated with positive interest in active and

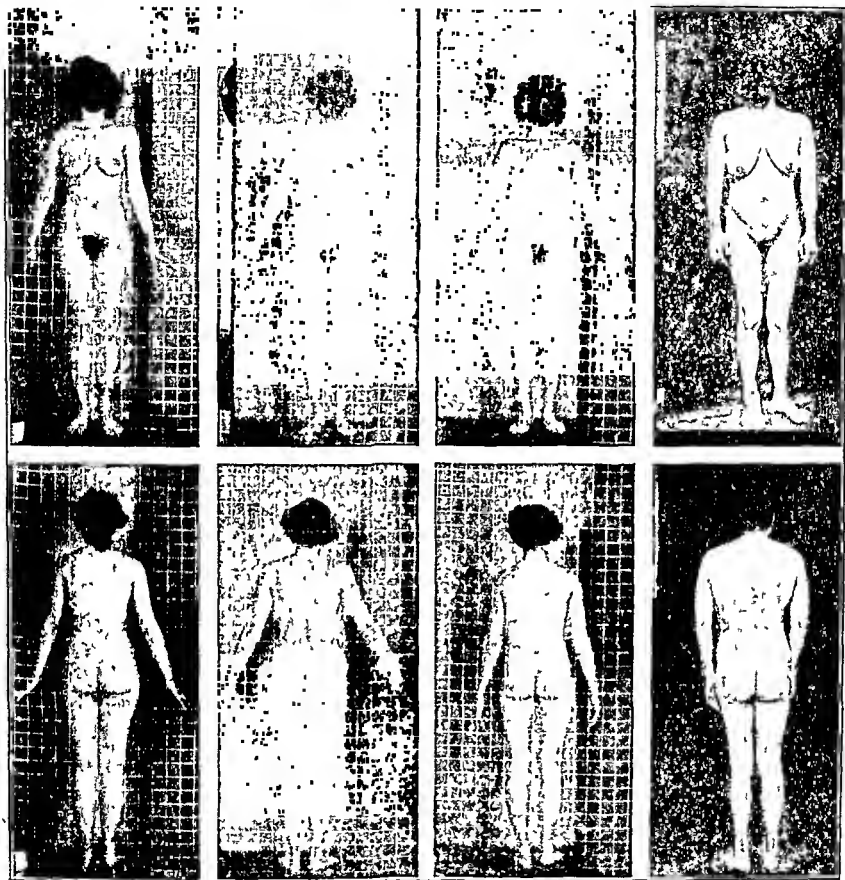


FIGURE 3 Showing Increasing Emphasis on the Andric Factor in the Female Morphology. (Figure at Right Illustrates a Case of Gulland Double Adrenal Tumor)

cence and conservation of energy, andric to its expenditure.

#### Psychology

In the psychologic panel, the task of differentiating andric and gynec characters is not altogether an easy one. Terman and Miles<sup>5</sup> undertook to assay the opposing qualities by means of various questionnaires and word-association tests. Their

mechanical pursuits, it is also associated with indifference to artistic and cultural pursuits. Femininity in men is the reverse of masculinity in its relationship to interests. Masculinity in women . . . is associated with positive rather than negative interests, with activity and, in the more highly educated, especially with intellectuality. Femininity in women shows the reverse of masculine trends. It appears associated with less intense positive interests and these are directed towards the arts of home and social life. Mental fem-



inity is expressed also in indifference to active scientific and in the better educated, intellectual interests.

There is, too, in the popular conception of maleness the quality of direction or leadership to which is applicable Murray's<sup>9</sup> term "regnancy." Or it might be called dominance, as opposed to the more commonly presumed feminine qualities of subservience and docility. Intelligence and reason, however, cannot justifiably be classed as essentially male; neither can intuition and emotion be allocated exclusively to women, for all these mental functions are extragenital possessions of every person. Some of these variable qualities no doubt are products of specific hormones. On the other hand, recognizable criteria of a different sort, perhaps conditioned, also seem to enter the picture. Thus, man's traditional notion of woman's nature and hers of his, and what in consequence each may expect of the other in the social and economic structure and in personal relations, inevitably stamp each with a reciprocally accepted cognition of sex. This picture, projected by a woman of what to her is a man, or by a man of what to him is a woman, varies widely in terms of racial, national and cultural background. Indeed, it seems to take on the order of an ethnic trait. Nevertheless, it is possible that from an infinite variety of blendings of andric and gynecic psychic values there may result preponderant projectivity or conservatism, determination or irresolution, directness or evasiveness, brutality or gentleness that will produce well-defined patterns of psychic personality. These may then be correlated with andric and gynecic qualities in the other panels of the total organism. The observable signs of these complete patterns are to be sought, not only in morphology and physiology, but also in the person's attitude toward life and in his manner of merging himself in his constantly changing environment.

#### CLINICAL APPLICATIONS

It was earlier suggested that if, instead of the genital mark, the androgynous mosaic were used as the criterion for division of individuals into sex groups, many of our present sex classifications in medicine might need revision. In this respect, the challenge offered to clinicians by the allocation of diseases according to sex is of greatest interest. There have been numerous studies of this matter; one of the most thorough being that of Mobius.<sup>10</sup> Moreover, in the textbooks of medicine, the paragraph on incidence usually states that the disease in question is commoner in one sex than in the other. After an exhaus-

tive inquiry in which he admits complete inability to explain the occurrence in men of diseases strikingly more frequent in women, Mobius concludes that if it were not for alcohol and syphilis, men would be less often sick and would live longer than women! Notwithstanding this naïve capitulation to a selected stress of environment, however, it should be noted that in his discussion of muscular dystrophies he remarks that muscle is notably "manly tissue; its failure difficult to explain."

That Nature apparently has more use for females than for males has long been known. From start to finish the latter show greater susceptibility to disease and a higher death rate. Thus, for example, studies of the sex ratio indicate that there are 160 early male abortions and 130 male stillbirths for every 100 female ones. Furthermore, at term, there are 104 or 106 living boys for every 100 girls who survive, but at the end of the first year, only 100 boys remain alive for every 103 girls. Bakwin<sup>11</sup> reports that among infants under one year of age 130 to 134 boys die for every 100 girls. This is a sweeping toll, which exists at a time when the genital phase of sex amounts to an almost negligible part of the total sex endowment. One gains the impression that the organismal or androgynous phase of sex must contain some curious relation between andric and lethal forces. One can accept, I think, as a limited factor against a man's chance of survival, Mobius's<sup>10</sup> belief that males are, in general, more exposed than girls and women to hazards, alcohol and syphilis. Also, it is known that developmental anomalies are commoner in males than in females, as though it were more difficult to build a male than a female. Thus, for example, in a series of 2000 cases of pseudohermaphroditism ten to one possessed the male gonad (Mobius). Furthermore, there is likewise that small group of rarer maladies that display the interesting phenomenon of sex linkage. The following conditions reported by Davenport<sup>12</sup> and others are dominant in males and recessive in females: coloboma, color blindness, night blindness, congenital nystagmus, ichthyosis, hemophilia, webbed toes and Gower's muscular atrophy. There remains, however, for further consideration a great group of more or less common diseases that appear year after year in the wards of general hospitals everywhere. Among these, one finds a varying incidence in men and women, changing from an equal distribution to more or less extremes of emphasis in one sex or the other.

Figure 4 charts a group of diseases that have been selected simply on the basis of their differ-



ential frequency in the two sexes. But it should be remembered that the figures are based on the concept of sex in terms only of gonad type. In other words, these are men because the gonad is testicular; those are women because they bear ovaries. The concept of the nongenital androgyny as a constitutional factor has not been introduced. Yet the very nature of the shifting curve apparent in the chart, which moves almost continuously from one sex preponderance to the other, suggests a susceptibility gradient rather than two diametrically opposed sex types. Furthermore, in many cases

there may be other gynec marks of contour, fat distribution, gesture, facial expression and turn of mind. Such men may be adequate sires, thus supporting their claim to masculinity in the genital phase. But in the rest of the organism strong gynec emphasis appears. One might infer from these considerations that as a general principle the more completely a person is differentiated toward maleness or femaleness, the less should be his or her predisposition for those diseases in which the opposite sex factor is a contributing one. Almost the reciprocal of the foregoing situation appears among the subjects of peptic ulcer, an illness in which the sex ratio is high, the ratio of men to women being 5 or 6:1. Here again the afflicted women usually possess evidence of andrie emphasis. It is interesting, too, to note that there is a tendency in ulcer families to produce a preponderance of male offsprings, whereas more female descendants appear in families of gallstone patients.<sup>13</sup>

In alcoholism the sex ratio is also high. Most statistics give the ratio of men to women as 6 or 8:1. But many observers will recall that the impression made by drunken women is a more masculine than feminine one. In my own experience with inebriates, almost every woman presented unmistakable emphasis on andrie characters. Interesting, too, is the fact that whereas for the whole alcoholic series men significantly preponderate, in Korsakoff's psychosis the ratio drops to 2:1. But I have not directly observed such cases in women for the purpose of evaluating the androgynous mosaic. This curious reversal of andrie-gynec emphasis in a special aspect of the human being's reaction to alcohol finds a parallel in rheumatoid arthritis and the spondylitis of Marie-Strümpell. Thus, in the general incidence of rheumatoid arthritis, 3 women are affected to 1 man. But in the cases of spondylitis, the ratio of men to women is 10:1. Heberden's nodes are found almost exclusively in women and, as originally pointed out by the great English clinician, usually at the climacteric. Such a phenomenon no doubt may be considered to be more directly determined by the hormone change (modification or curtailment) than by the original balance of somatic cellular androgyny. The age factor likewise must enter the picture, but much is still to be learned concerning the biologic relation of age and sex.

Gout, on the other hand, is almost entirely confined to the masculine sex. Concerning the androgynous balance of patients with this malady, I have met some difference of opinion. Two of my colleagues tell me that of the few female

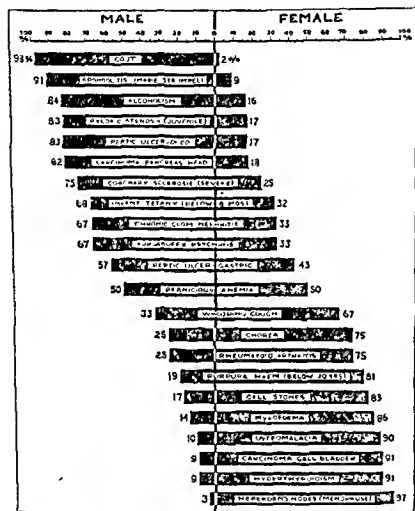


FIGURE 4. Differential Sex Incidence in Disease Susceptibility.

it has been possible to show that persons of one sex who develop a disease commoner in the opposite display notable emphasis on the inappropriate androgynous component of their own.

The scope of this paper does not permit a detailed discussion of each disease shown in the chart so that only two or three will be offered.

The patient with gallstones is one example. It is generally considered that women are more prone to the disease than men, in the proportion of about 5 or 6:1. Moreover there is an old medical saying that the commonest type of woman to be affected is "fair, fat and forty." When, however, a man who is the subject of cholelithiasis appears, one is often struck by the strong emphasis on gynec characters in his total person. In addition to evidences in skeletal measurements

gouty patients whom they have seen all presented strong emphasis on gynec features, with minimal emphasis on the andric. On the other hand, Jamieson<sup>14</sup> refers to Motley's picture of Margaret of Parma, "with her imperious temper, her masculine appearance, her moustache and her gout." It is possible that in my colleagues' cases the andric emphasis was much less marked in the morphologic than in the other panels.

When one attempts to explain the possible significance of disease incidence in relation to androgyny, the notion arises that the nature of the disease may express the different manner of energy manipulation that was earlier associated with each sex. Thus, men are commonly more vulnerable to diseases involving the apparatus for spending energy in action, whereas those that are related to energy storage and resting tissue metabolism arise chiefly in women. From the point of view, then, that sex appears to be a fundamental quality of somatic tissue, apart from its genital purpose, it is possible to contemplate the susceptibility to certain diseases as a further example of such bisexual somatic endowment.

Perhaps this dual possession may also be a mixed blessing. Concerning external agents, no doubt, andric or gynec properties do determine many patterns of reaction to life that are necessary or appropriate for the good of the individual man or woman. In primitive societies, however, the necessity for division of labor between man and woman for the care of offspring called out the opposite characters of each in widely separate spheres of action. All the outgoing energy production of the man was required to provide food, to build his cabin and to fight in defense of his home and family. The woman's energy on the other hand overflowed serenely through the house, surrounding her young with benevolent protection. Her instincts kept the larder jealously stored. Her swift intuition was alert to sense approaching danger; threatening problems were met out of stored experience by a remarkably successful empiricism. At that stage of history, men had comparatively little use for gynec qualities, or women for andric, so far as problems of adjustment to environment were involved. But these more or less unused opposite characters have become valuable to each sex with the increasing mechanization of contemporary civilization. Struggles of man against Nature have given place to those of man against man, and have confronted the individual with new kinds of adaptation demands. More and more, all occupations are being invaded by both sexes. In some of these, women are forced to swing their latent andric

factors into action; in others men must employ their gynec values. Police officers, business executives and lawyers, for example, are callings that attract women whose androgynous mosaic is highly colored with andric emphasis. The culinary art, horticulture, nursing and, finally, the practice of medicine are occupations toward which men lean when their gynec values are well developed. Of these, medicine is one of the most interesting. For many years it has been followed almost exclusively by men. Yet it is quite obvious that much of the success of the physician depends on his gynec values of intuition, understanding and impulse to conserve. It may be because of woman's increasing perception of her latent andric forces in the intellectual field that she now is entering the medical profession in steadily mounting numbers.

The purpose of the foregoing remarks has been to point out that this balancing pair of opposites—an Heraclitean enantiodromia—presents no cause for shame or embarrassment, but rather contains important values for every individual of each sex. Consequently it would be well if each person could recognize his or her androgynous pattern and permit its andric or gynec components to function appropriately in respect to the momentary life situation.

There is, however, a further sphere in which these two powerful forces may interact, not with environment, but on one another within the isolation of the self. Here in the innermost citadel, where the ego strives to preserve its essence, threats to the inviolability of the personal identity are challenged and parried. The intensity of this protective response is often reflected in the most extreme and grotesque compensatory efforts. These result apparently because for the average man there is no threat to self-preservation more potent than the implication of inadequate or declining virility. The notion that feminine qualities are inherent in his personality is one not easily accepted by most men. An excellent example of the early appearance of this sort of emotional distress is that which appears in boys who tend to plumpness and whose external genitalia develop slowly. And it has been my experience that such children never wholly lose the sense of inferiority established in those early days, notwithstanding subsequent achievement of physical and functional genital adequacy. Individual effort, however, to compensate for a deep psychobiologic awareness of essential inadequacy is a matter that is exceedingly difficult to evaluate mathematically. It remains inevitably individual,

an infinite variable. At present, it cannot be brought into the same statistical category with the morphologic and physiologic observations herein reported. But the principle may be illustrated by the effort of a certain soldier in World War I to satisfy himself that he was secure in the biologic sense. He was a congenital eunuchoid whose gracile form displayed the delicate nonmuscular contours of a young girl. He was accepted for service, and soon found himself an infantryman at the Chateau Thierry front. Not content with holding his place in the line, he requested the special duty of messenger between the advanced observation posts and the trenches. This peculiarly dangerous and fatiguing task he performed with distinction. On his return to peacetime occupation in America, the first job he selected was that of a ship loading longshoreman.

Of somewhat similar nature is the interesting observation that a majority of our peptic ulcer patients are drawn from the ranks of taxi cab drivers, policemen and firemen. These occupations demand constant output of energy in aggressive and often dangerous effort. Consequently, it is understandable that all these occupations expose their representatives to inner doubts concerning the validity of their essential beings. The intensity of these doubts may well relate to the actual balance of the andric and gynec forces that is present within the individual, and to his constitutional sensitiveness to the threat of his gynec component. From this conflict arises a fear in the subconsciousness of the potential peptic ulcer patient, for example, that when the crucial test comes he will fail to play the masculine role adequately for the preservation of either his body or his soul (ego?), or both. Now it has been my observation that among these patients the emphasis on the gynec component, especially within the psychological panel, has been unusually high—a paradox of the nature of the employment.

\* \* \*

Thus, it appears that, in respect to external agents, andric and gynec forces possess highly spe-

cialized and harmonizing reaction potentials. But within the person the two factors may come to grips with one another in destructive conflict. The intrinsic male fear is of his gynec component, which, if he could but accept and understand it, might prove instead to be a powerful ally. In view of these considerations, it becomes easier perhaps for each man and woman to appreciate how important to successful negotiation of life relations is an awareness, if not a complete understanding, of the phenomenon of androgyny. No doubt the andric and gynec factors, like other individual endowments, serve a biologic purpose. But depending on a person's repudiation or acceptance of them, they may become the source of destructive conflict or reservoirs from which energy may be wisely released toward creative work and equanimity.

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## PNEUMONIA IN MASSACHUSETTS: 1900-1940

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THE advances recently encountered in the treatment of pneumonia have been so spectacular that we have not dared to take our eyes from the road ahead, lest we fail to negotiate another sudden turn. Yet behind us lie facts that must not be forgotten, because they concern themselves with the very road over which we have been traveling, and there is no more useful way to visualize our progress than to retrace the actual path by which we have come. Modern pneumonia discussions have concerned themselves principally with selected groups or selected problems within the larger mass of the people as a whole. This is as it should be, for only by such selection can facts be established in detail. The experience of an entire population as expressed by its mortality figures, on the other hand, may be utilized to demonstrate the mass reaction of millions of people to the respiratory hazards of their environment. Although such experiences must be cautiously interpreted for pneumonia in Massachusetts, it is proper and may be profitable to speculate concerning the degree in which current habits and efforts have influenced the great changes that have taken place. It is especially pertinent to examine these relations while they are still fresh in mind.

To present a simplified concept of our pneumonia experience, the mortality curve for "all forms" of the disease has been chosen for illustration. Although this choice is open to criticism on several grounds, I believe that there is no better index of what has actually been occurring in Massachusetts. Morbidity rates are notoriously unreliable and incomplete. The separation of the lobar pneumonia cases is still accomplished by criteria on which the clinician and the pathologist do not always agree, and probably has more to do with the speed of invasion and the intensity of reaction within the host than with the circumstances of definition. Whether one prefers a clinical, anatomic or even a bacteriologic definition of lobar pneumonia, one will find that its curves pattern themselves very closely after that established for all forms. It is also of interest that the same pattern has been followed by the curves for measles, whooping cough and other

respiratory infections, each of which may appropriately be considered an integral part of the curve for all forms, and to have come under the same influences that have operated on the others. The accompanying chart (Fig. 1) is therefore considered the best available illustration of the behavior of pneumonia—including lobar pneumonia

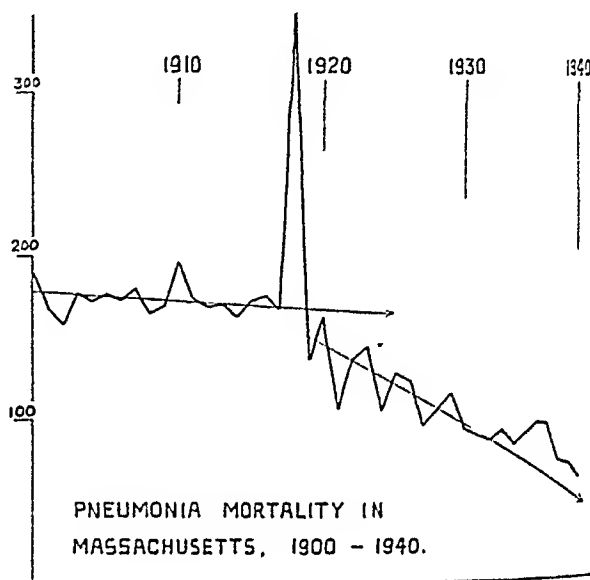


FIGURE 1.

—in Massachusetts for the present century. In addition, the curves for the registration area of the United States closely parallel this curve.

During the first seventeen years of the century, the pneumonia death rates were relatively constant. The total variation in Massachusetts was less than 15 per cent, and the trend was but very slightly downward. Then the epidemic of 1918 showed on what an unstable basis the relation between the pulmonary system and the outside world rested. The more one looks at this chart the more one appreciates the difficulty of estimating the influence of cause and effect in this disease. Involved explanations are needed to show why other clinics could not duplicate the therapeutic results achieved with unconcentrated serum at the Hospital of the Rockefeller Institute<sup>1</sup> in 1917; why two successive years in a single clinic led to opposite conclusions on the value of serum therapy, as they did on the pneumonia service at the Boston City Hospital<sup>2</sup> in 1920 and 1921; and why the general practitioners of medicine

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exhibited seeming indifference to what the enthusiasts of twenty years ago considered the great therapeutic contribution of the day. State-sponsored serum treatment was begun in 1919 in Massachusetts. In the light of what has happened, it is well that serum therapy was not universally adopted at that time, for it would now be difficult to escape a correlation between such an adoption and the very evident change in the mortality trend that took place (Fig. 1).

In the decade between 1920 and 1930, a remarkable series of reductions in pneumonia mortality occurred, reaching a point that was 50 per cent lower than the average of the first two decades. The trend of the curve for these ten years turned so sharply downward that it would, if projected, cross the base line in 1950! Of course the prospect of any such projection is fantastic, but it is important to remember that the major part of the reduction of the last forty years took place in this one decade. Whether the influenza epidemic had removed people with pulmonic susceptibilities, as has been suggested, or whether the general nutrition and resistance of the population were enhanced by changed habits and living standards is mere speculation. Better treatment may have been a factor, but not specific treatment, because very little serum was used in Massachusetts during this period; nor was any other therapeutic method employed on a large scale. One recalls enthusiastic claims for physical, chemical and biologic agents, but none of them enjoyed sufficiently widespread use to be reflected in this experience of the population as a whole. Most clinicians will agree that the therapy of the 1920 to 1930 decade was highly empiric, but that under it pneumonia somehow became a kindlier disease. Comment began to be heard on the mildness of the pneumonia seasons. The florid pneumonias, with full lobar distributions that lasted for a week or more, still occurred, but less frequently, whereas the abortive one-day or two-day pneumonias appeared, or at least were recognized more generally.

After 1930, it was plain that the pneumonia rates in Massachusetts could not continue along the trend that had been established for them following the influenza epidemic of 1918. There were too many people in the older age groups for whom pneumonia was a friend. As Osler<sup>3</sup> said: "Taken off by it in an acute, short, not often painful illness, the old escape those cold gradations of decay that make the last stage of all so distressing." The Massachusetts rates were also already lower than those of most other parts of the country, but as one recalled the explosion of

1918 one had a sense of insecurity. It was like an Indian summer: one was sure that it could not last. It probably would not have lasted if the present effective methods of treatment had not developed in rapid succession.

During the first five years of the Massachusetts Pneumonia Study,<sup>4</sup> from 1931 through 1935, the volume of serum treatment was not high; 793 cases were treated, and the total of pneumonia deaths in the State was 19,309—a ratio of approximately 1:24. During the next two years, 1936 and 1937, serum was given in 957 cases, and the total deaths amounted to 8394—a ratio of 1:8. This was the first period in which anything approaching an effective volume of serum therapy was applied in Massachusetts, and yet this treatment was accompanied by mortality rates that, in 1936 and 1937, were higher than they had been since 1930. This is true both with the figures for lobar pneumonia and with those for all forms. It may mean that the Indian summer was coming to an end in 1936. Those who collaborated in the Pneumonia Study believe that the rates would have been higher still, had not a comprehensive program of serum administration been under way. It therefore seems to be a fair conclusion that in 1936 and 1937 the pneumonia program minimized what might otherwise have been a greater natural variation toward seasons of increased pneumonic severity.

This is a point of more than academic interest, and it should be made at this time before one forgets just what really did happen between the two wars. The major part of the mortality reduction was spontaneous and rapid, and had nothing to do with antipneumonia efforts. It was due to natural causes, if living standards and habits may be included in this category. After 1934, a reaction in the severity of the disease occurred. It would probably have been a greater reaction, had it not been curbed by the gathering power of the pneumonia program. In 1938, with rabbit and other serums for the higher types of pneumococci, in 1939 with sulfapyridine, and in 1940 with sulfapyridine and sulfathiazole, the curve was again brought to new low points.

The rate for 1940, 61.6 per hundred thousand population, is the lowest yet recorded in Massachusetts. The amount of serum dispensed by the State was 40 per cent less in 1940 than in 1939. There is no such accurate measure of the amount of sulfonamide drugs used in 1940, but common knowledge would place its volume well above that of 1939. In other words, the best results were coincident with an increased usage of drug and

a decreased volume of serum treatment. This means that the community as a whole benefited by the large-scale application of a relatively safe and inexpensive and easily administered drug, the exhibition of which did not need to wait for bacteriologic study. The simplicity here implied may be open to scientific criticism, but it remains a practical fact, and suggests that a more effective anti-pneumonic treatment for the population as a whole had been awaiting the discovery of a method that would be simple enough for general application. The application of an involved science is as ineffectual as that of an involved art.

It has been said, "There was a steady drop, year by year, in the deaths . . . since the pneumonia programs began."<sup>5</sup> As an unqualified statement, this is debatable. The mortality record so far does show a steady drop since the use of sulfonamide therapy began. The record also shows that the spontaneous amelioration of pneumonia is the outstanding phenomenon of the century to date. This same natural amelioration is plainly written into the mortality returns for all the air-borne infections, including that chronic one—tuberculosis. Our respiratory security, if we have any, must rest largely on this natural foundation. It is the basis of a better health level for the people as a whole. Its versatility embraces all the air-borne diseases, and its total benefits are manifold. Even after excluding smallpox and diphtheria, which have been artificially prevented, the natural amelioration of the air-borne infections is already contributing a greater share to the prolongation of life than that provided by the almost complete elimination of the enteric fevers. For some reason, this epidemiologic similarity in the behavior of the air-borne diseases has never been commented on. Much has been said of the lessened severity

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Thus, there is much evidence to confirm a belief that during the present century pneumonia has been increasingly confronted by a collective resistance in the host. Early in the last decade, this resistance stabilized the pneumonia death rates in Massachusetts at a level 50 per cent lower than that of the first decade of the century. The pneumonia program and especially the widespread application of chemotherapy have now contributed to a still further depression of the death rates from pneumonia.

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## THE FREQUENCY OF POLIOMYELITIS IN PREGNANCY\*

W. LLOYD AYCOCK, M.D.†

BOSTON

INDICATIONS of the widespread and more or less uniform dissemination of the virus of poliomyelitis are seen in such epidemiologic features as the geographic prevalence and age distribution of the disease; in the gradation from frank to mild or suspected abortive forms of the clinical disease; and in the far more extensive occurrence of subclinical infection, as indicated by the development of serologic immunity in those who do not have the disease in any of its recognized forms.

The limited and selective occurrence of the frank disease indicates that some added circumstance determines clinical or subclinical infection on exposure to the virus. Certain of these selectivities point to differences in the person exposed rather than differences in exposure. A tendency to familial occurrence indicates that susceptibility may be inherent; seasonal and climatic variations in the frequency with which exposure to the virus results in the paralytic disease points to a physiologic function rather than to a fixed anatomic character; the association of the disease with persons of a certain constitutional type is suggestive of endocrinologic differences; the occurrence of poliomyelitis following surgical procedures on the upper respiratory mucosa indicates that temporary mucous membrane conditions may affect susceptibility; and, finally, because of the implication of the upper respiratory mucosa as the portal of entry of the virus, the suspected selectivity seen in the association of poliomyelitis with pregnancy, in view of known mucous-membrane alterations due to estrogenic changes of pregnancy, suggests that autarcologic susceptibility to poliomyelitis may reside, at least in part, in the economy of estrogenic substance.

As is well known, pregnancy affects the development or progress of a number of diseases, either favorably or unfavorably. These effects may be secondary to mechanical influences of the gravid uterus, they may be due to nutritional stresses, or they may result from intrinsic physiologic

changes, more specifically some of the marked endocrine changes of pregnancy. Thus, the improvement seen in certain cases of pulmonary tuberculosis has been ascribed to mechanical effect, such as splinting of the thorax; whereas the severity and fatality of pneumonia are perhaps less

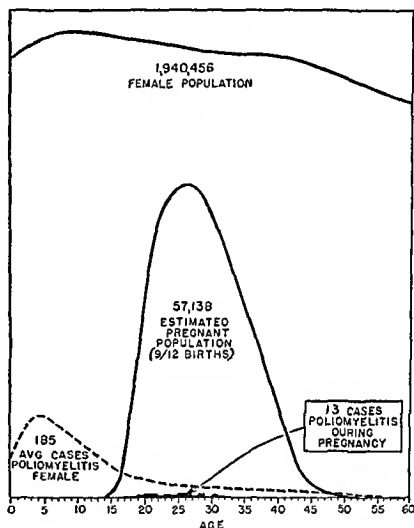


FIGURE 1 Expected Poliomyelitis during Pregnancy in Massachusetts

clearly attributed to immobilization of the diaphragm by the gravid uterus. The added nutritional demands may induce polyneuritis in patients already on a minimal diet, or this deficiency disease may be secondary to hyperemesis. Physiologic changes, including increased blood dilution and volume and increased cardiac output, with decreased hemoglobin, serum protein, non-protein nitrogen and red cells, account for the effects on heart disease. Certain endocrine disorders are initiated by, or are a continuation of, endocrine changes of pregnancy: toxic goiter may be activated, and pituitarism may be influenced. In still other diseases, no satisfactory explanation

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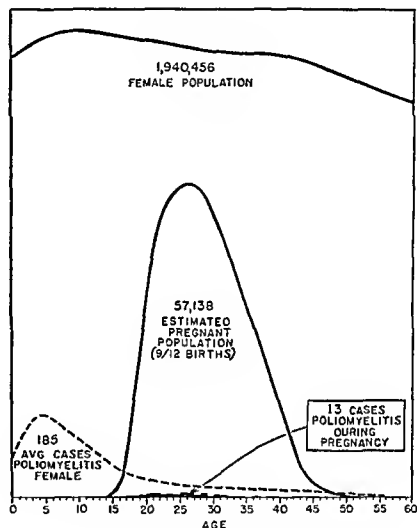


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is forthcoming for the effects noted. The mechanism of the so-called "therapeutic effect" of pregnancy on syphilis, as well as the resistance exhibited by pregnant animals to experimental infection with syphilis, is unknown. Because of the frequency of association, pregnancy has been regarded by some as an important predisponent to lethargic encephalitis.<sup>2, 3</sup>

The numerical infrequency of paralytic poliomyelitis, especially in view of the fact that the disease is preponderantly one of younger age

pregnancy is less than 1 out of 1000 cases of poliomyelitis, and less than 1 out of 50,000 pregnancies.

In reviewing the literature, 28 cases of poliomyelitis associated with pregnancy have been encountered, and an additional 28 cases have come to notice either by observation or personal communication (Tables 1 and 2). Since these cases have been collected incidentally, no estimate of the frequency of poliomyelitis in pregnancy can be drawn from them. A good many represent individual case reports, and some have been mentioned

TABLE 1. *Cases of Poliomyelitis in Pregnancy from the Literature.*

CASE NO	AUTHORITY	PLACE	AGE OF PATIENT	TIME OF ONSET	OUTCOME
			yr	mo.	
1	Vickman <sup>4</sup>	—	27	6th	Death (6th mo)
2	Schell <sup>5</sup>	Philadelphia	26	7th	Normal delivery
3	Hartman <sup>6</sup>	—	—	7th	—
4	—	—	—	7th	—
5	—	—	—	8th	—
6	—	—	—	5th	—
7	—	—	—	9th	—
8	—	—	—	4th	Death (4th mo)
9	Mueller <sup>7</sup>	Nauru	—	9th	Normal delivery (term)
10	—	Nauru	—	9th	Normal delivery (term)
11	Renault and Martigny <sup>8</sup>	—	23	5th	Normal delivery (term)
12	Zimmermann <sup>9</sup>	Germany	22	9th	Normal delivery (term)
13	Miller <sup>10</sup>	—	—	3rd	Normal delivery (term)
14	—	—	—	5th	Cesarean section (6th mo), death of child
15	Ehrenfest <sup>11</sup>	Missouri	18	6th	Normal delivery (term)
16	Hornung and Creutzfeldt <sup>12</sup>	Germany	20	8th	Cesarean section
17	McGoogan <sup>13</sup>	Nebraska	24	3rd	Normal delivery (term)
18	—	Nebraska	32	3rd	Normal delivery (term)
19	—	Nebraska	24	3rd	Premature delivery, death of child
20	Brahdy and Lenarsky <sup>14</sup>	New York	22	9th	Forceps delivery
21	—	New York	23	4th	Normal delivery (premature)
22	—	New York	19	2nd	Abortion (therapeutic)
23	—	—	—	Post partum (5 days)	Symptoms in child (9th day)
24	Guttmann <sup>15</sup>	Silesia	23	8th	Death
25	Pette <sup>16</sup>	—	—	3rd	Death
26	Klein and Sittig <sup>17</sup>	Germany	25	9th	Normal delivery
27	Morrow and Luria <sup>18</sup>	New Jersey	28	5th	Forceps delivery (term)
28	Ruhl <sup>19</sup>	Germany	27	8th	Normal delivery (term)

groups, makes its chance occurrence in pregnancy small. The average annual occurrence of poliomyelitis in Massachusetts for the ten-year period 1928-1937 was 455 cases, of which an average of 185 cases were in females. The number of births and stillbirths in the same population per year is approximately 76,000. Three-fourths of this number represent an approximation of the number of women pregnant at a given time. On a basis of the age distribution of poliomyelitis and the age of pregnancies, the estimated coincidence of the two conditions, as shown in Figure 1, at any given age is fractional, the total for all ages being 1.3 cases per year. But since this estimate is based on the incidence of poliomyelitis, of which only half the cases were paralytic, it may be seen that the expectancy of paralytic poliomyelitis in

in connection with other studies of the disease. The incompleteness of the record of poliomyelitis in pregnancy is further suggested by the fact that in the literature certain cases diagnosed as the well-known polyneuritis of pregnancy,<sup>20</sup> because of residual paralysis or fatal outcome with respiratory paralysis, possibly were actually cases of poliomyelitis.

The only outbreak in which the frequency of poliomyelitis in pregnancy has been studied was in Detroit in 1939.<sup>21</sup> A total of 528 cases were recorded, of which 255 were paralytic. Four cases occurred during pregnancy. In Table 3 are shown the female population, the estimated number of pregnancies, the expected coincidence of poliomyelitis with pregnancy, and the observed cases in the various age groups. Although this occur-

rence is over four times the expectancy, the number involved is too small to be considered conclusive. But the finding is in line with other evidence presented, suggesting that pregnancy may be one of the predisposing influences to paralytic poliomyelitis.

This suspected selective occurrence is in accord with other selectivities suggesting that susceptibility to paralytic poliomyelitis may reside in a disturbance of some physiologic function, which may be subject to fluctuations in the patient, is endocrine in nature, and is operative through ef-

enhance resistance to intranasal instillation of virus<sup>22-23</sup> It is not known whether, on the one hand, the particular preparation used, the dosage and the manner of administration were sufficient to give changes that could be considered optimal so far as enhancement of resistance is concerned; or whether, on the other hand, such changes are entirely artificial and quite beyond what could be expected to exist naturally. However, since the experimental observations agree with epidemiologic implications, it is believed that the artificially induced conditions may perhaps be

TABLE 2 *Cases of Poliomyelitis in Pregnancy from Personal Records*

CASE NO	PLACE	AGE OF PATIENT	TIME OF ONSET	OUTCOME
1	Vermont	37	7th	—
2	Vermont	32	7th	—
3	New York	25	Post partum (5 days)	Child born 1 me
4	Michigan	—	6th	Low forceps delivery (chloroform)
5	Massachusetts	—	9th	Cesarean section (7th mo) death of child
6	Massachusetts	—	Post partum (1 day)	Poliomyelitis in child (12 days)
7	Massachusetts	30	4th	Cesarean section
8	Massachusetts	19	5th	Premature delivery paralysis and death of child
9	Ohio	Young	2nd	—
10	—	—	4th	Abortion (7th mo) dead fetus
11	Florida	16	4th to 5th	—
12	New Hampshire	23	9th	Premature delivery (6th mo) death of child
13	Ireland	—	—	—
14	—	20	6th	—
15	Vermont	—	6th	Cesarean section (8th mo) death of mother and child
16	Massachusetts	35	6th	Normal delivery (term)
17	Massachusetts	24	5th	—
18	Maine	—	—	Cesarean section
19	Iowa	33	5th	Forceps delivery
20	New Jersey	27	5th	Forceps delivery
21	Vermont	26	8th	Normal delivery (term)
22	Illinois	22	9th	Respiratory paralysis forceps delivery and death of mother
23	Colorado	26	1th	Normal delivery (term)
24	Massachusetts	23	7th	Respiratory paralysis death of mother and child
25	Michigan	24	3rd	Normal delivery (term)
26	Michigan	16	6th	Normal delivery (term)
27	Michigan	26	1st	Cesarean section (5th mo) death of child
28	Michigan	26	7th	Cesarean section

fects on mucous membrane. The known mucous-membrane changes in pregnancy, which are attributed to estrogenic changes, and the experimental production of alterations in the genital and nasal mucosae of monkeys by the estrogens, —because of the implication of the nasal mucosa as the portal of entry of the virus of poliomyelitis, —have formed the basis of two sets of experiments in an attempt to determine the nature of the factor responsible for susceptibility to paralytic poliomyelitis. tests of the effect of artificially induced changes on the susceptibility of monkeys to intranasal instillation of virus, and comparative urinary estrogen assays on poliomyelitic patients and normal persons

The injection of estrogenic substance into castrate immature female monkeys was found to

considered as reflecting conditions of resistance in the natural disease. A small number of comparative urinary estrogen assays have been done on poliomyelitis patients and normal subjects. The results indicate a higher excretion of estrogenic substance in the group of poliomyelitic cases.<sup>22</sup>

The question may well be raised why, if the administration of estrogen protects castrate monkeys, the higher excretion of estrogen found in poliomyelitic cases and characteristic of pregnancy should not confer a similar benefit. No convincing answer can be given. It may be noted, however, that the hormonal status of the pregnant woman differs from that of the nonpregnant, as well as the castrate animal, in a variety of ways. For example, pregnancy is dominated more by the corpus luteum hormone than by estrogen

Pituitary growth-hormone secretion, as well as prolactin, is enhanced during pregnancy. It may be stated, in short, that the end effect of several interacting variables, one of which may be increased estrogen, might actually be different from increased estrogen alone. In this particular case,

TABLE 3. *Paralytic Poliomyelitis in Women, Detroit, 1939.*

AGE	FEMALE POPULATION*	ESTIMATED NO. OF PREGNANT WOMEN	NO. OF FEMALE PARALYTIC CASES	EXPECTED CASES IN PREGNANCY	OBSERVED CASES IN PREGNANCY
3+					
0-5	71,971	0	34	0.0	0
5-10	73,271	0	36	0.0	0
10-15	66,871	11	26	0.004	0
15-20	63,866	1,389	8	0.174	1
20-25	76,394	5,426	7	0.497	1
25-35	153,462	10,852	4	0.283	2
35-45	118,797	3,950	0	0.0	0
45-55	64,840	75	0	0.0	0
Totals	689,472	21,703	115	0.928	4

\*Based on figures for 1930 census.

the administration of estrogen to castrate animals approaches the latter condition, whereas conditions in the natural disease involve the interaction of a number of hormones, of which increased urinary output of estrogen may be only one manifestation.

### SUMMARY

Seasonal, climatic, familial and constitutional selectivities in the distribution of paralytic poliomyelitis among those exposed to the virus point to differences in the persons exposed rather than to differences in exposure. Bulbar poliomyelitis following tonsillectomy and adenoidectomy, in view of the implication of the upper respiratory mucosa as the portal of entry of the virus, suggests this mucosa as the seat of operation of susceptibility.

Fifty-six cases of poliomyelitis associated with pregnancy are cited, 28 from the literature and 28 from personal records. The time of pregnancy when the disease occurred is unknown in 2 cases. Only 9 cases were recorded in the first trimester of pregnancy, whereas 19 cases were in the second trimester and 23 in the third. Three cases occurred post partum. Thus, the latter months of pregnancy appear to be chiefly concerned, although it must be borne in mind that the data for the first months may be discrepant.

The manner of collection precludes statistical analysis, but it is estimated that the chance coincidence of the two conditions is roughly 1 in

1000 poliomyelitic cases and 1 in 50,000 pregnancies. In a study of the frequency of poliomyelitis in pregnancy in the Detroit outbreak in 1939, the estimated expectancy of coincidence was less than 1 case, and 4 cases were observed. The suspected association with pregnancy, in view of accompanying mucous-membrane alterations due to estrogenic changes, suggests that autarcologic susceptibility to poliomyelitis may reside in the economy of estrogenic substance. Experimental effects of estrogenic substance on susceptibility to intranasal instillation of virus are in accord with this concept.

Because of the difficulty in establishing the significance of numerical frequencies in studies of this sort, the present report is intended to raise the question of the frequency of poliomyelitis in pregnancy, in the hope that similar studies will be made in other outbreaks.

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## CLINICAL NOTE

AN ELASTIC CHEST GIRDLE  
FOR RIB FRACTURES\*

HAROLD G. LEE, M.D.†

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THE treatment of fractured ribs by adhesive strapping is so generally accepted, and on the whole is so satisfactory, that I have hesitated to report a retentive chest girdle used in treating such injuries. However, since for several years the girdle has proved to be a more comfortable form of treatment than the conventional strapping, as well as a more efficient means of immobilizing the chest, it seems to have special value. The girdle also has the advantage of being adaptable to cases in which the use of adhesive strapping is definitely contraindicated.

The idea of using a girdle to immobilize rib fractures is not new, although this form of treatment has received little recognition, and the use of the girdle has tended to be limited to those cases in which adhesive strapping is objectionable. Immobilizing belts and girdles of various designs and materials have been recommended by Knowles,<sup>1</sup> Funston,<sup>2</sup> Hammond,<sup>3</sup> Waugh,<sup>4</sup> Welti<sup>5</sup> and Christensen.<sup>6</sup>

In our clinic, the girdle is used in the treatment of all fractured ribs. When more than a single rib is broken, the position is maintained by increasing the width of the binder. The use of the girdle solves the problem of treatment when burns or abrasions are associated with the fracture, when the patient has a hairy chest or a tender skin, or when the respiration is embarrassed.

Patients find the binder extremely comfortable, and they promptly return to work. No pain is experienced on movement of the thorax, and there is no feeling of constriction, such as that when adhesive strapping is used. The man who does heavy work may tighten the binder during the day and loosen it at night. Immobilization is

assured, because there is no tendency for the girdle to slip, as there is with adhesive strapping.

A more detailed description of the elastic girdle than that given in Figure 1 is hardly necessary. In width, it varies from 10 to 20 cm., depending on

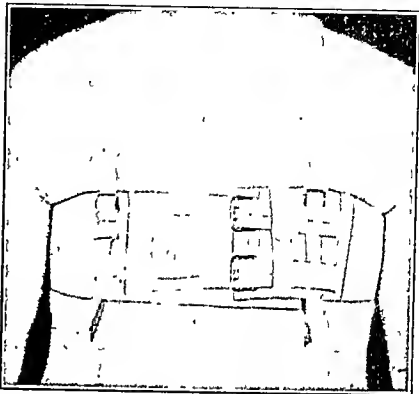


FIGURE 1. Elastic Girdle Applied to Chest.

the number of ribs fractured. The girdle is easily and quickly made from readily obtainable material, and it costs very little. It is easily fitted, since the elasticity and the long range of buckling space allow for adjustment to a chest of any size. In its application, it should be tightened until there is no pain on forced inspiration or expiration. Because of the ease of adjustment, the girdles may be made in advance and kept on hand. When sufficient healing has taken place to ensure immobilization at the site of the fracture, the girdle is gradually loosened, and finally removed.

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## MEDICAL PROGRESS

## DIABETES MELLITUS

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BOSTON

## STATISTICS

THE death rate for diabetes in the United States reached 25.6 per 100,000 in 1939, with a total of 33,395 cases, thus exceeding 23.8, the previous highest figure, which was attained in

TABLE 1. *Deaths per 100,000 Population from the Chief Causes of Death in the Registration Area of the United States in 1939, as Compared with the Figures for the Same Causes in 1938 and 1900.\**

DISEASE	1939		1938		1900	
	RANK	RATE	RANK	RATE	RANK	RATE
Heart disease	I	276.1	I	268.9	IV	132.1
Cancer	II	117.8	II	114.6	VIII	63.0
Cerebral hemorrhage	III	88.0	IV	85.7	VII	71.5
Nephritis	IV	83.1	V	77.2	V	89.0
Violence (accidents, suicides and homicides)	V	70.9	III	94.1	VI	96.0
Pneumonia	VI	59.4	VI	67.5	II	180.5
Tuberculosis (all forms)	VII	47.2	VII	48.9	I	201.9
Diabetes	VIII	25.6	IX	23.8	XVII	9.7

\*Prepared with the co operation of the Statistical Bureau, Metropolitan Life Insurance Company.

1938. One death in 41.5 was assigned to diabetes. In 1938, diabetes ranked ninth as a cause of death, but by 1939 it displaced premature births and became eighth. The positions held by diabetes in 1900, 1938 and 1939 are shown in Table 1. It requires little imagination to see that diabetes will soon displace tuberculosis and pneumonia, and then it will be exceeded only by arteriosclerosis in the heart, brain and kidneys, and by cancer and violence. Yet this very growth in incidence may detract from its recognition, because so few diabetic patients die of their disease that other diseases—which are complications or coincidental, like cancer and tuberculosis—may claim recognition before it and displace diabetes as the primary cause of death. Private clinics may therefore be the chief source in the future of reliable statistics on the disease. For statistics on diabetes, the seventh edition of Joslin, Root, White and Marble's<sup>1</sup> book on the treatment of diabetes mellitus presents recent data in considerable detail.

All articles in this series will be published in book form, the current volume is *Medical Progress Annual, 1940* (Springfield, Illinois: Charles C. Thomas Company, 1941 \$4.00).

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The number of new cases for the year 1940 is estimated at between 50,000 and 60,000 by Mr. Herbert H. Marks, of the Statistical Department of the Metropolitan Life Insurance Company.

The remarkable alteration in the age distribution at death of diabetic patients in the United States for the last twenty years is shown in Table 2. There were approximately only one fifth as many deaths in the first decade of life in 1939 as in 1919, one fourth in the second and third, one third

TABLE 2. *Percentage of Deaths from Diabetes, Classified according to Decade of Age at Death, in the Registration Area of the United States in 1919 and 1939.\**

AGE	1939			1919		
	TOTAL %	MALES %	FEMALES %	TOTAL %	MALES %	FEMALES %
Under 10	0.6	0.9	0.5	2.9	3.4	2.5
10-20	1.6	2.0	1.3	5.2	6.2	4.3
20-30	1.5	2.0	1.2	5.4	6.2	4.6
30-40	2.2	2.6	1.9	6.1	7.1	5.2
40-50	6.4	6.7	6.3	10.0	10.2	9.8
50-60	18.7	17.3	19.5	21.0	19.8	22.0
60-70	33.0	30.9	34.3	27.4	25.8	28.8
70-80	28.3	29.0	27.8	17.7	16.8	18.4
80-90	7.3	8.2	6.7	1.1	4.1	4.1
90-100	0.4	0.5	0.4	0.3	0.3	0.2
Number of deaths	33,395	12,558	20,837	12,683	5,769	6,914
Death rate per 100,000	25.5	19.1	32.0	14.9	13.3	16.5

\*Prepared with the co operation of the Statistical Bureau, Metropolitan Life Insurance Company.

in the fourth, three fifths in the fifth, and six sevenths in the sixth; not until the seventh decade are deaths now more numerous. Conversely, there were 33 per cent more deaths in 1939 in the tenth decade, nearly 80 per cent in the ninth decade and 60 per cent in the eighth decade.

The median age at death of patients with diabetes in New York City is advancing. Between

TABLE 3. *Median Age at Death of Diabetic Patients in New York City.*

PERIODS	MEDIAN AGE AT DEATH			
	MALES		FEMALES	
	Lowest	Highest	Lowest	Highest
1904-1921	56.1	59.1	58.2	61.0
1922-1940	59.2	64.7	60.4	65.4

1904 and 1921, inclusive, and between 1922 and 1939, inclusive, there was a significant change equivalent in range to three to five years for men and two to four years for women, owing largely to the introduction of insulin (Table 3).

For 927 deaths occurring, in the experience of Joslin, Root, White and Marble, between January 1, 1937, and March 29, 1940 (the Hagedorn Era), the average age at death was 64.8 years, and the duration of the disease 12.5 years, in contrast with 46.7 years and 6.1 years, respectively, for the period June 1, 1914, to August 6, 1922 (the Allen Era).

The total number of persons with diabetes in New York City is estimated to be somewhere between 50,000 and 75,000, or 6.8 to 10.2 per 1000 population.

In a systematic study based on reports of the physicians of the Berlin Medical Society, Umber and his associates<sup>2</sup> report that in the population of Berlin (4,346,074) there were 14,153, or 3.2 per 1000, diabetic persons—in 1916 in Charlottenburg, the estimate was 2.3 per 1000. Insulin was used in the treatment of 37 per cent. The necessity of supplying insulin to diabetic patients to increase their working capacity has been stressed by Umber's group. In the diabetic clinic of the West End Hospital in Berlin, only 3 per cent of patients were unable to work on account of their disease. The number of Jews in Berlin was estimated at 82,788, and among them 3.5 per 1000 were diabetic; insulin was used by 43 per cent.

### EDUCATION

The present is the Era of Education in diabetes. Two large monographs on diabetes have recently appeared, along with an increasing number of schoolbooks, textbooks and manuals for patients. Camps for children are far more numerous, exceeding eighteen in number, and probably are more largely attended. The number of articles on diabetes, whether clinical or experimental, is so voluminous that a reviewer is swamped and sometimes almost breathes a sigh of relief to see a periodical that has nothing related to diabetes on its pages.

Boards of health are increasing their diabetic activities, and in New York City last winter more than two hundred popular talks on the disease were sponsored by the Board of Health, in co-operation with medical societies. For some years, Cincinnati has been particularly active in this regard. In New York City many years ago, Dr. Charles F. Bolduan was largely instrumental, working from his position in the Board of Health, in bringing about, with the help of the New York Academy of Medicine, the organization of the New York Diabetes Association.

More instruction in diabetes is given in hospitals. More nurses are engaged in teaching diabetic patients, and more classes have been organized

for their benefit. In addition to this work for patients, more time is set aside for the study of diabetes in nurses' training schools and in medical schools.

Insurance companies have a vital interest in diabetes. This year, one of them has undertaken an educational program that is nationwide in scope and on a broader and yet more detailed basis than has ever before been attempted. It is evident that the interest not of one but of many insurance companies is being awakened. Their accurate statistical methods are sorely needed in diabetes. It would be even more valuable if they made a searching inquiry into the deaths reported as diabetic and the deaths of persons who earlier were known to have had diabetes.

For several years in England, there has been an organization for diabetic patients known as the Diabetic Association. It issues the *Diabetic Journal*,\* sold for a shilling, which contains practical articles on diabetes suitable for patients and the public. The association and the *Journal* continue to function despite the war.

During the last few months, the American Diabetes Association has been incorporated, its first meeting was held in Cleveland last June preceding the meeting of the American Medical Association. This society is national in scope and is best described by Articles II and III of its constitution:

**ARTICLE II Purpose** The objects of this association are (1) to disseminate among physicians information relative to the diagnosis and treatment of diabetes by means of meetings, bulletins and the publication of papers in scientific journals, and through a central office, which would at all times make available information concerning various aspects of diabetes, (2) to educate the laity in the early recognition of diabetes and in the realization of the importance of medical supervision, (3) to secure and co-ordinate the active co-operation of associated groups acceptable to the Trustees in the educational and organizational phases of the association, (4) to make and publish statistical surveys of diabetes, (5) to encourage and support clinical, experimental, sociological and statistical studies by means of grants, (6) to encourage the adequate treatment of diabetes and the establishment of summer camps for children.

**ARTICLE III Membership** The membership of the association shall consist of four classes: (1) active members, (2) associate members, (3) honorary members, (4) corporate members. Only active members in good standing shall have the right to vote. Any physician with proper qualifications may be elected an active member of the association by a majority vote of the Trustees. Active members shall pay stipulated annual dues. All those interested in the aims and purposes of the association, whether physicians, scientists, statisticians, dietitians, nurses, social workers or laymen, may become associate members upon election.

\*The *Journal* is published quarterly at 124 Baker Street, London, W. 1.

by the Trustees, and upon payment of stipulated annual dues. Honorary membership may be conferred by the Trustees on those individuals who have rendered distinguished services in medical or other fields related to diabetes. Associated medical or welfare organizations, civic or educational groups and insurance companies may be elected to corporate membership of the association in recognition of the auxiliary services which they may render to the association.

### *The Prevention and Cure of Experimental Anterior-Pituitary Diabetes*

In last year's review,<sup>3</sup> reference was made to the unpublished work of Haist, Campbell and Best,<sup>4</sup> of Toronto, and of Lukens and Dohan,<sup>5</sup> of Philadelphia, on the prevention and cure of the experimental pituitary type of diabetes of the dog and cat. To recapitulate briefly, Best and his co-workers found that when insulin was injected into a dog at the same time as anterior-pituitary extract, diabetes failed to appear, and no destructive changes occurred in the islands of Langerhans; Lukens and Dohan observed in a cat with experimentally produced diabetes, even of five months' duration, that hydropic degeneration, the incipient diabetic lesion, which had appeared in the island cells, was reversible, and the diabetes could be cured with insulin. Cure in the cat was related to the peculiar persistence, characteristic for that animal, of the hydropic degeneration.

Dohan, Fish and Lukens<sup>6</sup> report two dogs resistant to the injection of anterior-pituitary extract, but following partial pancreatectomy without associated glycosuria, permanent diabetes resulted as soon as a small amount of extract was administered. Two other dogs were made permanently diabetic after sixty-two and ninety-eight days of treatment with small but fairly constant doses of extract. In dogs made diabetic with anterior-pituitary extract, the diabetes may be so severe that 85 per cent or even more of the available glucose of the diet is excreted in the urine, but if these dogs are treated with insulin, the rate of progress of the diabetes seems to be inhibited.

The blood glucose in dogs with moderate and severe pituitary diabetes, sixteen to twenty-four hours after the last feeding, varied widely and showed little relation to the proportion of the available glucose of the food excreted in the urine. It appeared to be a poor index of the severity of the diabetes.

The concentration of serum fatty acids was above normal in the severer cases of diabetes, being particularly marked in dogs excreting 90 per cent of the available glucose of the diet. There was no correlation between the quantity of ketonuria and the concentration of the serum fatty

acids in individual determinations. The withdrawal of insulin combined with fat or meat feeding resulted in a marked increase in the concentration of serum fatty acids. The cessation of insulin treatment with fasting was associated with very little change. Meat feeding, in comparison with that of fat, brought about a marked ketogenic effect.

Some animals did not show permanent recovery with insulin treatment. These cases were associated with infections, poor control of the diabetes by insulin or the institution of insulin treatment after more than five months of diabetes.

In last year's review,<sup>3</sup> it was considered that the prevention and cure of the experimental disease were attained primarily by the use of insulin, which permitted rest to the pancreas by the removal of excessive metabolic strain. Subsequently, however, Best and his co-workers<sup>4</sup> not only confirmed the previous observation of Housay that the hyperglycemic effect of anterior-pituitary extract was not obtained in fasting dogs, but also noted that the feeding of fat had a similar effect in thwarting the action of the diabetogenic factor in the extract. Fasting and the feeding of a high-fat diet are not only reminiscent clinically of the fasting era of diabetic treatment introduced by Allen and of the high-fat diets advocated by Newburg and Marsh in this country and by Petrén in Sweden, but also corroborative of their rational employment as therapeutic agents.

Still more recently, Lukens and Dohan<sup>5</sup> have added another means to the three already known—insulin, fasting and high-fat diet—to be effective in the prevention and cure of experimental diabetes, and with its discovery have afforded an explanation of the action of each of the four. This fourth measure is the use of phlorhizin. Phlorhizin does not decrease the sugar in the urine or indeed the production of sugar, but actually lowers the sugar in the blood by removing it. For the four procedures, a normal—that is, a low—blood sugar represents the greatest common divisor. And here again support is found for the persistent, aggressive and, one might add, orthodox treatment of diabetes originally advocated by Naunyn. We consider the clinical effects of this work far reaching.

Cantilo,<sup>7</sup> in the Argentine, has treated 40 diabetic women in the menopause with large doses of sex hormones, to influence the diabetogenic factor in the pancreas. He considers that he obtained a constant improvement of the state of all who showed evidence of disturbed hormonal balance, as shown by hyperpituitarism and as measured by the dextrose-tolerance test. He empha-



sizes the need of separating the climacteric from the usual type of diabetes. Successful responses were obtained only with large doses of estrogen and progesterone. Conversely, the use of androgens has been reported as lowering carbohydrate tolerance,<sup>8</sup> and Dr F P Pyles, of Brazil, in a personal communication, refers to a patient whose usual tolerance for 300 gm carbohydrate was lowered to about 100 gm while 25 mg testosterone propionate was being taken.

A pancretotropic as well as diabetogenic factor exists in the anterior portion of the pituitary gland, and it has even been suggested that the former by stimulating the islands to secretion might explain why, in the production of anterior pituitary diabetes, signs of recovery are repeatedly manifest in the early steps of the injections. Collip<sup>9</sup> has offered evidence on this point, using a primary alcoholic extract of anterior pituitary tissue. Marks and Young<sup>10</sup> could not confirm his work. Although there is such a factor, they found that it was not identical with prolactin or with gonadotropic, thyrotropic or glycotropic substances. Indeed, they surmise that this principle is not a hormone. Lawrence and Young,<sup>11</sup> by experiments on diabetic human beings and on dogs permanently diabetic with pituitary extract, also failed to confirm Collip's views.

Young<sup>12</sup> attempted to answer the question whether the treatment of an animal with large doses of estrogen would inhibit the liberation from the anterior lobe of the pituitary gland of certain specific hormones and thus influence the course of diabetes. He used dogs made diabetic by injections of anterior pituitary extract. The administration of large doses of estrone, estriol and diethylstilbestrol to four pituitary diabetic dogs and one that had been depancreatized exerted no obvious antidiabetic action. In fact, with estrone and estriol, the effect was prodiabetic rather than antidiabetic. Young discusses the fact that his results are in disagreement with some earlier results of other authors.

These negative attempts to isolate a pituitary hormone that will offset the diabetogenic pituitary hormone have been failures, but it seems well worth while to continue the search. Haist, Campbell and Best<sup>4</sup> write: "The hope is raised that proliferation without degeneration, produced by the administration of anterior pituitary extract along with adequate amounts of insulin, may lead to an increase in the islet tissue and a more nearly normal islet fraction." Indeed, Marks and Young<sup>13</sup> have recently shown that certain anterior lobe extracts increased the insulin content of the rat's pancreas to almost twice normal values.

Encouraged by the reports of the Toronto and Philadelphia laboratories in preventing diabetes in a dog and curing it in a cat, McDaniel, Marble and Joslin<sup>14</sup> reviewed their cases in the hope of finding clinical evidence of prevention or cure. They sought these in the group showing hydropic degeneration of the islands. In human beings, however, fulminating diabetes is infrequent, and it is especially rare to have a fatal case since the introduction of insulin. Warren<sup>15</sup> had only 22 cases of hydropic degeneration among 486 autopsies on patients with diabetes. Light of these and a later case were from the George F. Baker Clinic. They included 2 patients carefully treated with a relatively or extremely low carbohydrate diet and insulin who died, we should now say needlessly, of diabetic coma, 1 with coma brought on by hyperthyroidism, 2 in whom cancer entered into the picture, destroying a portion of the pancreas, 3 with infections and 1 with an uncertain duration who died suddenly in coma. Among the cases with a sudden onset, cures were not found in children whose diabetes was not recognized until they were in coma, in prepubertal and adolescent children, in women whose diabetes began in pregnancy or in the menopause, and in the large group of elderly diabetic patients, although some cases of unusual improvement were observed. Yet the search did disclose hints that made the authors urge still more aggressive, active and consistent treatment of the disease with the reduction of carbohydrate and the use of insulin.

#### ACIDOSIS AND FAT METABOLISM

Certain recent experiments have discredited four of the former basic concepts of fat metabolism and ketogenesis.

First, Knoop's<sup>16</sup> hypothesis of successive beta oxidation, which he described in 1904, has been discarded, and in its place Hurler's<sup>17</sup> hypothesis of multiple alternate oxidation of the fatty acid chain, in which simultaneous oxidation occurs along the entire chain at alternate carbon atoms with the formation of ketones, has been accepted.

Secondly, the ketone bodies, which were formerly considered to be toxic and unavailable for use in the body, have now been shown by Chaikoff and Soskin,<sup>18</sup> Friedemann,<sup>19</sup> Stadie, Zapp and Lukens<sup>20</sup> and others to be the normal end products of fatty acid oxidation and to be utilized in the peripheral tissues by both normal and diabetic subjects. It is only when the ketone bodies accumulate owing to the excessively rapid breakdown of the fatty acid molecules—as in diabetic acidosis, when insulin is inadequate—that the

ketones form more rapidly than they can be utilized and have a toxic effect, because their acidic properties disturb acid-base equilibrium, electrolyte balance and water exchange.

The third revolutionary change is the discarding of the old idea that ketones can be oxidized only by obligatory coupling with carbohydrate oxidation. The experiments of Barker<sup>21</sup> with depancreatized dogs and of others show that fat may be completely oxidized without coupling with carbohydrate oxidation.

The fourth hypothesis—that fatty acids are converted into glucose in the liver—was disproved by the experiments of Stadie, Zapp and Lukens<sup>20</sup> with liver slices of diabetic cats.

At present, Stadie<sup>22</sup> believes that part of or all the fatty acids catabolized undergo a preliminary partial oxidation in the liver to acetoacetic or beta-hydroxybutyric acid. These ketone bodies can be used without chemical coupling with carbohydrate oxidation. He also believes that during exercise the utilization of the ketone bodies keeps pace with their increased formation.

Stadie further believes that the greater the carbohydrate metabolism, the less the fat metabolism.

By actual analysis of total bodies of mice, MacKay and Drury<sup>23</sup> showed that ten times as much of the carbohydrate fed was stored as fat than as glycogen. Fat is ordinarily the great energy reservoir of the body. Drury<sup>24</sup> holds that one of the actions of insulin is to facilitate the formation of fat from carbohydrate and thus to store carbohydrate in its most efficient form.

#### TREATMENT

The need for adhering to adequate standards of treatment and control of diabetes is still to be emphasized. Hyperglycemia and glycosuria, as well as acetonuria, are abnormalities that the most seasoned students of diabetes have always sought to correct. As Allen<sup>25</sup> points out, hyperglycemia must denote an insulin deficit, because it is absent in normal persons on identical diets. In the management of diabetes in children, Jackson, Boyd and Smith<sup>26</sup> based their treatment on the premise that physiologic levels of control (normal blood-sugar levels, freedom from glycosuria or insulin shock, and completely adequate diet) are desirable and attainable. It must be admitted, however, that their children remained for comparatively long periods in the hospital. Evidently, in the series of 800 cases described by Smith and Grishaw,<sup>27</sup> standards of treatment and control were orthodox. In a group of 247 obese diabetic patients, the disease was moderately severe in 79 and mild in the remainder, but when reduction in weight was established, the number of moderately severe cases became 32.

Present-day tendencies in dietary treatment seem to be definitely in the direction of moderation with respect to the total amount of carbohydrate fed. Thus, the New England Deaconess Hospital diets containing 140 to 175 gm. of carbohydrate are certainly more commonly used than diets with 200 gm. or more. Our experience has clearly indicated that a smaller dose of insulin is thus required, and that the tendency to hypoglycemic reactions is less. Dr. Allan M. Butler,<sup>28</sup> at the Children's Hospital in Boston, also favors the lower carbohydrate diet and gives an excellent table showing a parallel between the amount of carbohydrate in the diet and the amount of insulin required in diabetic children.

#### CONSTANCY OF ACTION OF PROTAMINE ZINC INSULIN

The constancy of the action of protamine zinc insulin is emphasized by Ricketts,<sup>29</sup> who showed that its effect when injected once every twenty-four hours is relatively constant, regardless of the time of day the injection is given. The best criterion for the proper dose is the fasting blood sugar, because protamine zinc insulin metabolizes endogenous carbohydrate. Supplementary crystalline insulin is often necessary before one or two of the daytime meals. Errors in the use of crystalline insulin should never occur, since the only form of crystalline insulin manufactured at present exerts an action that is rapid and comparable with regular insulin, but is not to be compared with the long action of protamine zinc insulin, histone insulin or globulin insulin. In general, most young patients and many with moderately severe diabetes need both crystalline insulin and protamine zinc insulin. A careful comparison of various methods of using these two forms of insulin is given by Watson,<sup>30</sup> and the conclusion is reached that the best results were obtained by the use of two types of insulin, separately injected.

#### ESSENTIAL FRUCTOSURIA

The importance of essential fructosuria lies in the fact that it is a harmless anomaly of metabolism sometimes mistaken for diabetes and therefore resulting in dietary restriction and the use of insulin in patients in whom neither is required. Lasker<sup>31</sup> has analyzed 40 cases in the literature and added 7 cases of her own. Apparently, this disorder is inherited as a Mendelian recessive, commonly found in the brothers and sisters of patients, but usually absent in the parents. It is essential to remember that fructose may be formed from dextrose in an alkaline urine by the process of chemical inversion. This can happen in a diabetic urine or a urine containing bacteria. Also,

in cases of deficient liver disease, fructose may be excreted in the urine after a test dose of sugar.

anism favoring the early and excessive development of arteriosclerosis.

#### ADVANTAGES OF EARLY DIAGNOSIS AND AGGRESSIVE TREATMENT

The advantages of the early diagnosis and aggressive treatment of diabetes lie in the preservation of a high tolerance. The point is well made by Dr. F. D. W. Lukens, who writes in a personal communication:

Diabetes has commonly been treated by diet with the least restriction possible, and then by insulin used as late as possible and in the smallest doses possible to control the metabolism. This may be called the principle of minimal treatment. It appears to be fairly suitable for the management of diabetes of long duration, but *at the time of first diagnosis*, at least if soon after onset, a different policy might well be adopted, namely, *early maximal treatment*. The feature underlying this method is that as soon as the diagnosis is made insulin should be given in the largest doses which can be tolerated without reactions. The advantages to be anticipated include: better education of the patient from the beginning; more prompt and complete control of the disease and its progress (by resting the pancreas?); and the possibility of preventing the condition from becoming permanent. The prevention of permanent damage to the pancreatic islands has not been demonstrated in man, although recent results in two laboratories show that this is possible in early experimental diabetes. It may be that well-equipped clinics will strive for such prevention in human beings albeit with the most sober expectations.

#### ARTERIOSCLEROSIS

The coexistence of arteriosclerosis with diabetes, particularly the occurrence of the severe form of occlusive arterial disease in patients in middle life and in diabetes of long duration, is an outstanding problem. Whether the excessive degrees of arteriosclerosis develop prematurely because of uncontrolled diabetes, or whether the tendency is due to an inborn, inherited trait, is still discussed. As a practical problem, it still remains true that the responsibility rests on every physician who treats diabetic patients to give appropriate instruction and treatment to avoid the accidental development of serious lesions, which may often be prevented from reaching a serious stage if early treatment is given. A valuable contribution is a recent account from the laboratory of Dragstedt. Dragstedt and his co-workers<sup>22</sup> found arteriosclerosis of the aorta in 11 depancreatized dogs, an incidence of 13 per cent. In 75 normal dogs, the incidence was 5 per cent. They noted that the dogs were given insufficient amounts of lipocaic to maintain normal fat metabolism, and they pointed to the disturbances of fat metabolism in the liver in diabetes as the mech-

#### INSULIN RESISTANCE

Extraordinary cases of resistance to insulin requiring doses of 1000 to 3000 units a day continue to appear. We<sup>23</sup> have observed two cases—those of a young clergyman and a nurse—in both of which, rather rapidly in the course of a few weeks, such a resistance developed that 2000 units of insulin were required; during the next year, the resistance gradually disappeared. In a case reported by Hart and Vicens,<sup>24</sup> a sixty-year-old Hungarian fruit dealer developed a general, as well as a local, allergic reaction lasting four days after the first dose of insulin. During the next few days, the insulin dose reached the maximum of 920 units. However, the insulin resistance disappeared within a few weeks, and subsequently the patient required no insulin at all.

In certain cases, allergy to insulin requires desensitization. The rapid method of desensitization by the injection every twenty to thirty minutes of very small doses, beginning with 1/100 unit and rapidly working up to several units in the course of four to six hours has been successfully used, but the method we have adopted in several recent cases and prefer has been to begin with 1/1000 unit and increase by 1/1000 unit at each dose before the three meals and on retiring; before breakfast 1/1000 unit, before lunch 2/1000 unit, before the evening meal 3/1000 unit and on retiring 4/1000 unit; occasionally, one can go ahead more rapidly. Patients who begin insulin and then omit it are especially prone to allergic complications.

Another case of severe insulin resistance in a patient with diabetes and chronic lymphatic leukemia is reported by Levi and Friedman.<sup>25</sup> This patient received 4000 units of insulin a day for four days, and 19,900 units over a period of five successive days. His white-cell count varied from 61,000 to 25,000. The possibility that in the large number of leukocytes a trypsinlike ferment was responsible for anti-insulin action was suggested. In a study of carbohydrate metabolism in 4 cases of insulin resistance by Root and Carpenter,<sup>26</sup> it was striking that in 2 cases, when glucose was given to the patient in the fasting state, almost no increase in the respiratory quotient was obtained. Yet with levulose the rise in the respiratory quotient within thirty minutes to an hour was practically equivalent to that found in normal persons. The highly specific character of the metabolic defect is as yet unexplained. In

these 4 cases, the striking feature was the cyclic character of the phase of insulin resistance.

### VITAMIN DEFICIENCIES

The place of vitamin deficiencies in diabetes continues to excite interest and to stimulate experiments. Brazer and Curtis<sup>36</sup> report a study of 20 patients with juvenile diabetes mellitus, all of whom were found to have poor light adaptation as shown by the Frober-Faybor biophotometer. The daily administration of 60,000 units of vitamin A in the form of fish-liver oil brought about a return to normal, whereas the use of crystalline carotene failed to bring about improvement. In discussing the various causes and explanations of these symptoms, they accepted the inability of the patient with diabetes to convert carotene to vitamin A. This seems to depend on some deficiency in liver function. That there is any specific relation between vitamin deficiencies and the causation of diabetes is still very doubtful. Owens, Wright and Brown<sup>37</sup> have confirmed earlier studies in finding that the administration of ascorbic acid to diabetic patients produced no change in the severity of the diabetes.

The relation of the peripheral neuritis of diabetes to vitamin deficiency is still somewhat uncertain. In a series of 422 ambulant diabetic patients, Fein, Ralli and Jolliffe<sup>38</sup> found 9 who had a symmetrical peripheral neuropathy similar to that found in patients who suffered from proved vitamin B<sub>1</sub> deficiency. The findings that served as a basis for diagnosis consisted in sensory changes in the lower extremities, such as hyperesthesia, tenderness of the calf muscles and loss of position sense and of vibratory sensation, beginning first in the toes and later extending upward, in addition to absence of ankle jerks. The daily administration of thiamine by mouth resulted in cure of 8 subjects and improvement in 1. Some adjustment in the insulin dose went on at the same time, and hence it is possible that diabetic treatment, as well as thiamin, played a part in relieving the condition. Indeed, the exact place of thiamin in the polyneuritis of alcoholism, pregnancy and even beriberi has been questioned by Meiklejohn.<sup>39</sup> He points out that the laboratory animals suffering from thiamin deficiency do not have a true peripheral neuritis but do have a disturbance of the metabolism of the central nervous system. His belief is that, when a true peripheral neuritis occurs, the treatment should include an ample and nutritious diet together with the administration of yeast and crude liver extract to

ensure an adequate supply of vitamin B complex. In the treatment of the neuritides associated with diabetes, when a vitamin deficiency is suspected, it is probably wise to use the complete vitamin B complex rather than thiamin alone.

One of the features of diabetic neuritis is the existence of an increased amount of protein in the cerebrospinal fluid without an increase in cells. This condition is characteristic of the Guillain-Barré syndrome or polyradiculoneuritis. A series of 15 cases of this type is described by de Jong.<sup>40</sup> In these cases, the total protein in the acute stage varied between 125 and 412 mg., with an average of 214 mg. for 100 cc. The average cell count was 6. The patients were quite young, the average being twenty-two years. The onset was rather sudden, and recovery occurred usually after an average of eight weeks. Slight infections had been present at the beginning in some cases. These cases differed materially from the diabetic cases that one sees clinically. Ordinarily, in diabetic patients, the onset is insidious, and in a fully developed case a young person's recovery frequently requires more than eight weeks. However, in severe cases, development of atrophy and contractures and a long duration of the neuritis were signs akin to what we see in diabetic patients. The fatal cases had bulbar involvement and respiratory failure.

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 27371

#### PRESENTATION OF CASE

A fifty-nine-year-old woman came under medical observation with the following story.

Twenty years previously, the patient had been treated for peptic ulcer, without recurrence of symptoms, and about this time she suffered a transient attack of thyrotoxicosis, which was treated with x-rays. The details of the latter illness were not available. Ten years later at the time of the menopause, she became mentally unstable, with symptoms referable to the gastrointestinal tract and heart and "a good deal of jointiness." For this illness, she visited several sanatoriums. Six years before, the patient had suffered from regurgitation of food shortly after eating, and at this time it was found that the heart was enlarged and that the liver extended two fingerbreadths below the costal margin; the latter was not tender, and the upper border reached the fifth rib. X-ray studies revealed a slightly enlarged heart and tortuous esophageal folds, with some delay at the cardia, but no varices could be demonstrated. The basal metabolic rate was +13 per cent. Approximately one year later, the patient suffered a transient attack of pleurisy, and for twenty-four hours a left pleural friction rub was audible. She carried on in fair health for four years, and during this time she was considered by successive physicians to be a neurotic patient whose regurgitation of food was not based on organic esophageal disease. Her insistence that she had heart trouble was denied by all. She complained of a good deal of "jointiness" in her hands, and these symptoms were thought to be due to degenerative arthritis, with hypertrophic changes at the joint margins, but no x-ray films were taken to prove this point.

However, for the summers of the previous three years, she had had "mosquito bites" which developed on the dorsal surfaces of the forearms, the jaw line of the face, and along the collar line near the sternoclavicular junctions. These lesions began as tiny, reddish, slightly elevated areas on which there soon developed a central scab. They itched, and the scab pulled off when scratched, leaving a small pit. The erythematous area widened to about the size of a dime, or even a quarter, with a large necrotic area

in the middle. These lesions disappeared in the course of four to six weeks, leaving a depressed white scar, with punctate areas in the scar that probably represented the site of hair follicles. Sometimes at the end of this period, after feeling somewhat giddy for several days, the patient suddenly developed "a lump between her breasts," and a sense of pressure aggravated by breathing and by lying flat or on the left side. This symptom was accompanied by mild nausea and inability to relax, and precluded sleep. It disappeared by morning but recurred the next day for a few hours. The patient had also noticed some shortness of breath on exertion. She had lost 15 pounds, and there was a stare to the eyes, with lidlag. The left border of the heart was 10 cm. from the mid-line in the fifth left interspace, and the first sound was described as "mushy," with a shuffling systolic blowing murmur. The heart beat was regular at a rate of 70, the pulmonic second sound being greater than the aortic, and at the lower sternum a scratchy sound was heard in systole that was believed to be extracardiac; the blood pressure was 144 systolic, 85 diastolic. The liver was palpable two fingerbreadths below the costal margin on deep inspiration, with its upper border at the fifth rib. Neurologic examination was negative. The skin lesions were present, but only in the form of depressed atrophic scars, no fresh lesions being noticed. The patient ran a low-grade fever for one week. X-ray films of the colon and gall bladder, as well as a Graham test, were negative; at the lower end of the esophagus a delay in passage of the barium was noted, with possibly some thickening of the mucous membrane, but it was not the picture of cardiospasm or cancer. Degenerative changes were present about the joints. An electrocardiogram revealed moderate left-axis deviation, with T-wave changes that were possibly due to digitalis or a combination of digitalis and coronary disease. The basal metabolic rate was +34 per cent.

A month later, repeated readings of the basal metabolic rate gave figures of +28, +39 and +36 per cent, so that the patient was given iodine, and in a few weeks the reading was +17 per cent. There was no palpable goiter or evidence of a sub-sternal gland by x-ray examination. Blood counts were normal, the sedimentation rate was high normal, and the stools were normal. The patient carried on for the next four months, gained 7 pounds and remained mentally well; she had very little regurgitation of food, but there was still some exertional dyspnea. At the end of this period, a sensation of weight developed in the anterior chest, and shortness of breath increased. On examination, she did not appear ill, but a to-and-fro

friction rub was heard over the precordium, base and apex, loudest over the left sternal border at the fourth interspace. The heart was regular at a rate of 96, with the same systolic murmur, and the pulmonic second sound was greater than the aortic; the blood pressure was 130 systolic, 90 diastolic. The liver was three fingerbreadths below the costal margin. The white-cell count was 8000, and the sedimentation rate 40 mm in one hour. An electrocardiographic recording showed marked left-axis deviation, a PR interval of 0.22 second and a QRS complex of .09 second,  $T_1$  and  $T_2$  were upright,  $T_3$  inverted, and  $T_4$  flat. The temperature had risen to 100°F. forty-eight hours later, but fell to normal in the next two days, and by this time the precordial friction rub had disappeared. The patient was kept in bed for one month, then gradually allowed up, but it was noted that the neck veins were distorted in recumbency, that there was an increase in dyspnea, and that a nonproductive cough occurred after meals and when the patient was lying in bed. She went to the country at this time, and within a week or two began to develop the aforementioned erythematous skin lesions. The patient's condition remained essentially unchanged for the next two months, at the end of which a rolling heave was observed over the precordium, which was transmitted to the liver region. The liver reached a point five fingerbreadths below the costal margin, but was not tender, the spleen could not be felt, nor were there other signs of congestive failure. Examination of the urine and blood was negative. Salycan produced a diuresis, but did not appreciably affect the exertional dyspnea or cough. A few weeks later, crackles were audible at the lung bases, more pronounced on the left; there was no visible or palpable pulsation of the liver.

On examination, the patient was well developed and well nourished, tired and weak, but mentally clear, with moderate exertional dyspnea, however, she appeared only slightly ill, and the temperature was normal. The cervical veins were distended; there was slight exophthalmos, but the thyroid gland was not enlarged. The fingers were thick and shiny, and the skin showed many small white scars and a few fresh, reddish, scabbed maculopapules on the hands, forearms, face and anterior neck. Examination of the heart showed enlargement to the left, with a normal rhythm at a rate of 80 and a bifid apical impulse. The pulmonic second sound was greater than the aortic, and there was a diastolic murmur at the apex and lower end of the sternum. The pulse was normal, the arterial walls soft, and the blood pressure 140 systolic, 95 diastolic. Persistent fine rales

were present at both lung bases, but no dullness. The liver was enlarged and tender, reaching four fingerbreadths below the costal margin; there was no peripheral edema. Examination of the urine and blood was negative. An electrocardiographic recording showed a normal rhythm at a rate of 80, and a PR interval of 0.24 second; there were low voltage of the QRS waves, flattish T waves and a deeply inverted  $T_1$ .

The patient was confined to bed and given vitamins, digitalis, weekly mercurial diuretics, a normal diet and limited fluids. She improved, but cardiac reserve hung in the balance, with gallop rhythm at the apex, pronounced accentuation of the pulmonic second sound and jugular pulsation. During the next few weeks, the patient had less respiratory difficulty and gained in strength, but new umbilicated papules appeared on the face and arms, edema of the legs developed, and the liver was palpable at the umbilicus. At the end of seven weeks, a protodiastolic gallop was heard maximally at the lower end of the sternum, and there were rales at the lung bases, the liver was firm and slightly tender, and had receded to the costal margin; new skin lesions appeared, the older ones becoming scarred. The urine contained an occasional hyaline cast with a trace of albumin, the blood was normal, with a sedimentation rate of 30 mm. in one hour. Within three weeks the patient began to lose ground appreciably; she developed anorexia, cough, increasing dyspnea and arthritis of the finger joints, and the temperature rose to 101°F. On examination, the fingers were spindled, and new skin lesions were present on the face, arms and legs. The heart findings were unchanged, rales were present at both lung bases, and the liver again reached the umbilicus. Gradually, edema increased in severity and grew more widespread, involving the hands and face; no longer was there response to mercurial diuretics, and jugular pulsation was visible to the ears. The patient became weak, her hands and feet were cold and purple, and the pulse was rapid and feeble, the temperature dropped to 95°F, and albuminuria increased. Occasionally, a curiously loud first or second heart sound could be picked up. Fresh pruritic skin lesions continued to develop and appeared as raised, gray-white, dry, scaly areas measuring up to 4 mm in diameter and surrounded by purplish margins, the whole averaging 1 cm. in diameter.

Terminally, there was little stupor, and death occurred quite suddenly, with deepening cyanosis, approximately six years after the discovery of cardiac enlargement. Fever was present almost daily for the last five months of life.

## DIFFERENTIAL DIAGNOSIS

DR. WALTER BAUER: Being, as Dr. Mallory knows, extremely interested in lupus erythematosus disseminatus I find it very difficult to get away from a diagnosis of that disease in this case. True, the patient was somewhat older than such patients usually are. However, we know it does occur at this age. Over a six-year period, this patient suffered from pericarditis, pleurisy, a recurring rash and, finally, arthritis. It is very difficult to say what caused the joint symptoms. They may have been due to degenerative joint disease. I believe that the patient suffered from mediastinopericarditis rather than simple pericarditis. The former is rare in disseminated lupus, but there are on record three cases that have had a well-defined mediastinopericarditis. There is no mention made in this record of whether she had a paradoxical pulse.

DR. MYLES P. BAKER: She did not.

DR. BAUER: Or whether the heart was fixed in position.

DR. BAKER: It was not.

DR. BAUER: And there is also no mention whether x-ray study showed anything but upward displacement on inspiration.

DR. BAKER: That was not looked for.

DR. BAUER: One wonders if the first episodes in this patient's history could not be accounted for on the basis of the same disease. I took the liberty to ask Dr. Aubrey O. Hampton whether the x-ray findings in the esophagus could be accounted for on the basis of mediastinitis. He stated that he did not know. In mediastinitis, "a rolling" of the esophagus is usually observed. I do not know whether the esophagus in this case showed such changes.

DR. BAKER: I should say not.

DR. BAUER: Dr. Hampton said there was nothing about the x-ray picture to lead one to suspect cardiospasm or intrinsic disease of the esophagus. This patient never had a Broadbent sign?

DR. BAKER: No.

DR. BAUER: One would think she would have had distention of the neck veins as the disease progressed.

DR. BAKER: I did not look for that.

DR. BAUER: The pleurisy could, of course, have been a manifestation of disseminated lupus. The recurrent rash each summer is very suggestive of disseminated lupus. There is one case on record of a patient who had recurring skin rash every summer for ten years except one and that was the year when he worked nights instead of days. There is another case on record of recurring skin

rash for four successive summers, with complete disappearance in between. Another point in favor of this diagnosis is the fact that some of the skin lesions left scars. The arthritis that developed terminally could have been a manifestation of the disease. Whether the original joint symptoms were related to this final illness, one cannot say. One might ask if it is not unusual to see pericarditis as the first sign of the disease. The answer is that it is unusual. However, visceral manifestations may be the first evidence of the disease, and we have seen one patient who had chronic crippling arthritis for ten or twelve years before developing skin lesions. Another had chronic arthritis for a period of four or six years before visceral symptoms became evident. Many of the classic findings may be absent. I think the distribution of the skin lesions in this case is consistent with the diagnosis. The patient had no evidence of the bone-marrow involvement that is sometimes seen in this disease, nor did she exhibit purpura. The absence of leukopenia should not disturb us, because only 30 per cent of our 65 cases had low leukocyte counts.

The patient never developed hypertension. The terminal urinary findings could be explained on the basis of mediastinopericarditis, which I believe she had. Should one consider the possibility of pericarditis from other causes? Did she have Pick's disease of tuberculous origin? One could explain the skin lesions, which resulted in scarring, on the basis of tuberculosis. It would, however, be extremely difficult to explain the arthritis in this manner.

One must mention periarteritis nodosa. It commonly causes pericarditis, which may be associated with mediastinitis. Some of the other findings observed in this case would not be so readily explained by this diagnosis, although we must admit that an additional case of periarteritis nodosa could have all the findings presented by this patient, including the arthritis. We have seen one patient with periarteritis nodosa with a marked synovitis. In this case, the typical vascular lesions of periarteritis nodosa were demonstrated in the synovial blood vessels. A primary vascular disease such as periarteritis nodosa of six years' duration would probably have affected the vessels of the pericardium, heart, cerebrum, abdomen or legs at some time during the course of the disease.

One might suspect rheumatic fever. The PR interval was prolonged—0.22 and, finally, 0.24 second. However, the skin lesions were not those of rheumatic fever. Rheumatoid arthritis can involve serous surfaces, but there seems little reason for seriously considering it in this case.

I consider disseminated lupus the best explanation.



tion of this patient's symptoms and physical findings. One might argue that mediastinal involvement is not in keeping with this diagnosis. However, I know it can occur. Therefore, I believe we were dealing with a patient whose mediastinopericarditis was part and parcel of the picture of disseminated lupus. Tuberculosis need not be seriously considered. Although periarteritis nodosa is a distinct possibility, I believe we can exclude it.

DR. TRACY B. MALLORY: Does anyone care to hazard a diagnosis or express an opinion?

DR. BAKER: This woman presented the picture terminally—indeed, during the last five months—of febrile illness and progressive right-sided heart failure, with accentuation of the pulmonic second sound, a finding that was difficult to explain. We believed that she had disseminated lupus, and in retrospect I doubt very much that she had a thyrotoxicosis. She had always had prominent eyes, with lidlag. I think that an elevation of the basal metabolic rate has been noted in disseminated lupus, presumably in a case in which fever was not prominent. I suspect we were on the wrong track in attributing an elevated basal metabolic rate to recurrent thyrotoxicosis. The difficulty as I saw her from day to day was how to explain the right-sided heart failure that was obviously taking her to her end. I could find no reference in the literature of disseminated lupus to right-sided heart failure, no definite description of myocardial disease that would account for such a picture. We considered the accentuated pulmonic second sound—the loudest heart sound—as evidence of chronic cor pulmonale.

DR. EDWARD F. BLAND: One could explain that with mediastinopericarditis.

DR. BAKER: But would one expect the meager heart sounds and the pronounced gallop rhythm?

DR. BLAND: I do not see why they need be anything more than evidence of a failing heart.

DR. BAUER: I do not see why an accentuated pulmonic second sound must necessarily be indicative of right-sided heart failure. Was she a slender person?

DR. BAKER: No, she was not.

DR. BLAND: I should be inclined to discount the finding.

DR. BAKER: What of the gallop rhythm?

DR. BLAND: It is a good sign of weakened myocardium, either on the right or left.

#### CLINICAL DIAGNOSES

Acute disseminated erythematosus.  
Cardiac failure.

#### DR. BAUER'S DIAGNOSIS

Lupus erythematosus disseminatus.

#### ANATOMICAL DIAGNOSES

Disseminated lupus erythematosus (probable).  
Idiopathic pulmonary endarteritis (Ayerza's disease).

? Periarteritis nodosa of pulmonary vessels.

Polyserositis: pericarditis, pleuritis, peritonitis.

Cor pulmonale.

Infarcts of lungs.

Healed pyelonephritis, slight.

Arteriosclerosis, aortic and coronary.

Lymphadenopathy, axillary.

#### PATHOLOGICAL DISCUSSION

DR. MALLORY: The post-mortem examination showed a polyserositis. There was turbid fluid in one pleural cavity. There were some old but loose adhesions and some extensive fluid in the pericardium, and there was 150 cc. of turbid fluid—a small amount—in the pelvic portion of the peritoneal cavity. The heart was hypertrophied, weighing 450 gm., but all the hypertrophy was on the right side, an extreme grade of cor pulmonale. The right ventricle measured from 7 to 10 mm. in thickness, and since it was also markedly dilated, that represents as marked hypertrophy of the right ventricle as I have ever seen.

DR. BAUER: The patient had left-axis deviation, according to the electrocardiogram.

DR. MALLORY: I am sorry about that, but I have no explanation to offer. The lungs were fixed whole by injection of formalin into the bronchial tree. Later, they were examined by means of numerous cross-sections. When the surfaces of these sections were examined under the dissecting microscope, it was apparent that every small artery was markedly thickened, many having no visible lumen, whereas the large arteries showed numerous and large plaques of atheroma. On microscopic examination, we found ordinary but severe atheroma of the large and intermediate-sized pulmonary arteries and more puzzling changes in the pulmonary arterioles. In many places, this was a fibrous, intimal thickening, sometimes evidently the result of thrombosis, organization and recanalization. In some arteries, fresh thrombi were still apparent. In others, the picture was more suggestive of an endarteritis. However, there were a significant number of vessels in the lungs in which the picture was still different. The media of these arteries was thick and necrotic. There was a periaarterial granulomatous process with polymorphonuclears and numerous monocytes, and the picture in these vessels was indistinguishable from periarteritis nodosa.

So far as the rest of the body is concerned, not a diseased arteriole was found, except for some

ordinary atheromatous changes in the heart and in the uterine vessels. The spleen was normal in size. The liver was considerably enlarged and deeply congested, with some central necrosis. The kidneys weighed 350 gm., a little larger than normal. There were a few patches of sclerosed glomeruli, a few dilated tubules filled with hyaline casts and a few lymphocytes suggestive of a very mild healed pyelonephritis. There were also, I think, a few glomeruli showing focal glomerulitis. Whether one could separate those entirely from the old pyelonephritis and attribute them to another process, I am not sure.

Most of the lymph nodes of the body were not enlarged. On external palpation, we did not feel any, but on dissecting into the axillas, we found on both sides a great many enlarged nodes, wet, pink and highly vascular. On microscopic examination, they showed great increase in blood vessels, and necrosis of the germinal centers, changes that we usually find in acute disseminated lupus.

Although a few vessels in the lung were characteristic of periarteritis nodosa, nothing else in the body favored that diagnosis; there were a number of clinical and a few anatomic points that fit better with the diagnosis of lupus.

## CASE 27372

### PRESENTATION OF CASE

An eighteen-year-old single primipara was referred to the hospital three weeks after delivery.

Two months before admission, the patient presented herself at the prenatal clinic of another hospital, where her condition was followed until the time of delivery. She had no untoward symptoms, and physical examination revealed nothing abnormal except minimal ankle edema; the blood pressure was 100 systolic, 80 diastolic, and the urine was normal. During the last six weeks of pregnancy, she gained 11 pounds, and at the time of the delivery was recovering from a cold. Three weeks before admission to this hospital, her child was born after a normal six-and-a-half-hour labor aided by an episiotomy, although it was stated that the patient lost slightly more blood than is usual. On the second post-partum day, the ankle edema was the same, but the face became pallid and puffy. The blood showed a red-cell count of 2,400,000 with a hemoglobin of 48 per cent, and a white-cell count of 16,000 with a normal differential. A Fouchet test was negative. The blood pressure was 100 systolic, 64 diastolic, and the urine was normal. The next day, edema was more marked, and the liver was palpable two fingerbreadths be-

low the costal margin and was somewhat tender. A catheter specimen of urine was strongly positive for albumin, had a specific gravity of 1.015 and contained many white blood cells; colon bacilli were cultured. The nonprotein nitrogen of the blood serum was 100 mg., the uric acid 14 mg., the cholesterol 181 mg., and the sugar 69 mg. per 100 cc.; the icteric index was 5. On the third and fifth post-partum days, transfusions of 500 cc. of blood were given. On two occasions intravenous injections of 100 cc. of 50 per cent glucose were given for anuria. The urine volume rose from less than 400 cc. to more than 1000 cc. The fluid intake was forced to 2000 cc., and the edema increased. At no time did the temperature rise above 99°F. During the eight days before admission, the white-cell count dropped from 35,000 to 21,000. The lochia was foul and persistent, but the uterus was said to have involuted satisfactorily with the aid of two courses of Ergotrate. Finally a small mass developed just lateral to the umbilicus between the lower edge of the liver and the fundus. The edema had slowly increased.

Four months before admission, the patient was in bed for five days with tonsillitis. Her physician painted her throat, and recovery was satisfactory. There was a history of occasional nocturia of several years' duration. The patient's menstrual periods had always been normal. The family history was irrelevant.

On examination, the patient responded slowly and was cyanotic and orthopneic. There was pitting edema of the entire body. She preferred to lie on her right side, her breath coming in shallow gasps, with occasional coughing. The tongue was dry, and there were sordes on her lips. The left arm was much smaller than the right and showed a large ecchymosis above the elbow. The trachea was slightly deviated to the left. Examination of the lungs revealed dullness, increased vocal fremitus and bronchial breathing over the entire right chest. Slight dullness was present at the left base, but the breath sounds were vesicular, with no rales. Examination of the heart showed the left border to be 1 cm. to the left of the mid-clavicular line. The sounds were somewhat distant, with occasional extrasystoles and an inconstant gallop rhythm; the blood pressure was 90 systolic, 68 diastolic. The abdomen was distended and edematous, and shifting dullness was present. The liver was palpable three fingerbreadths below the costal margin. The fundus of the uterus reached a point 3 cm. above the symphysis pubis. Pelvic examination revealed a septic perineorrhaphy, oozing pus. The uterus was in second-degree retroversion, enlarged and slightly fixed. The vaults

were clear. The pupils were dilated, but reacted to light and accommodation. The fundal vessels showed slight narrowing. Examination of the nervous system was negative.

The temperature was 102°F, the pulse 90, and the respirations 30.

Examination of the urine showed a specific gravity of 1.026 and a ++ test for albumin; the sediment was "loaded" with white blood cells and contained an occasional granular cast. A culture grew abundant colon bacilli. Examination of the blood showed a red cell count of 5,000,000 with a hemoglobin of 13.5 gm. (photoelectric-cell technic), and a white-cell count of 21,000, with 82 per cent polymorphonuclears. The nonprotein nitrogen of the blood serum was 63 mg. and the serum protein 4.6 gm. per 100 cc.; the chlorides were 914 milliequiv. and the carbon dioxide combining power 16.5 milliequiv. per liter. A serum van den Bergh was biphasic and slightly above normal. A vaginal smear was negative for beta-hemolytic streptococci; a throat swab showed a few colonies of beta hemolytic streptococci.

An x-ray film of the chest showed a large amount of fluid on the right side and less fluid on the left. The outlines of the diaphragm and heart were obliterated by the fluid. Nothing could be said about the size of the heart or the condition of the lungs. A flat abdominal film showed marked enlargement of the soft tissues of the abdominal wall, consistent with edema. The psoas shadows were poorly outlined, the kidneys incompletely visible. There was an unusual stripy appearance of the abdomen, perhaps due to edema in the retroperitoneal tissues, which accounted for the poor demonstration of the kidney and psoas shadows.

An electrocardiographic recording showed normal rhythm, with a rate of 90 and a PR interval of 0.15 second. T<sub>1</sub> was flat to inverted, T<sub>2</sub> and T<sub>3</sub> were inverted. There was slurring but no abnormality of the QRS complex.

On the day of admission, the right chest was tapped on two occasions, and yielded 250 cc and 800 cc of slightly cloudy, straw-colored fluid. This fluid had a specific gravity of 1.011, contained 3300 red blood cells and 58 white blood cells per cubic millimeter, clotted in five minutes on standing, and yielded no growth. After this procedure, the patient was more comfortable. On the second hospital day, the temperature was 100.5°F, the white cell count 12,000, and the blood pressure 100 systolic, 60 diastolic. An electrocardiogram showed auricular premature beats with a rate of 85 to 90 and a PR interval of 0.19 second. There was slurring of the QRS complex and moderate right axis deviation. T<sub>2</sub> was diphasic,

T<sub>3</sub> inverted. The next day, the patient was placed in an oxygen tent, remained uncomfortable, but was apparently holding ground. The blood pressure dropped to 70 systolic, 45 diastolic. Despite five blood transfusions of 500 cc. each and general supportive measures, the patient rapidly failed, with steadily increasing edema, cyanosis and dyspnea. Death occurred on the sixth hospital day.

#### DIFFERENTIAL DIAGNOSIS

DR FULLER ALBRIGHT "A Fouchet test was negative," whatever that is.

DR. TRACY B. MALLORY The reagent is a mixture of trichloroacetic acid and ferric chloride, which is a strong oxidizing agent and turns bilirubin green. The test is usually applied to urine.

DR. ALBRIGHT. I should like to be sure that the urine was normal in all other respects on the second post partum day. If so, it would rule out many things. One must always remember that specimens can be mixed.

The fact that the liver was apparently enlarged is not particularly significant because of the relaxed abdominal wall from the recent pregnancy.

The anemia was controlled by transfusions.

"A throat swab showed a few colonies of beta-hemolytic streptococci." It would be much more interesting to know whether it was negative for pneumococcus.

I have listed seven things that I shall consider, but only the last two do I consider very seriously. The first is post partum eclampsia. The patient did not have hypertension. I do not think it was eclampsia. The second thing is a colon bacillus pyelonephritis. She was sick on the second day after delivery, and the urine was said to be normal at that time. If that was true, she was not sick because of pyelonephritis. Besides, there is not so much albumin in the urine with pyelonephritis, and her course was much too rapidly downhill for uncomplicated pyelonephritis, and I rule it out as the primary disease. I do not believe that she died of colon bacillus pyelonephritis or septicemia. The next possibility is pneumococcal pelvic infection, with secondary nephrosis, for which one can make a fairly good story. Again, if the urine was normal on the second post-partum day, it would rule out this diagnosis. The patient did have the nephrotic syndrome—at least, a great deal of albumin, a low serum protein with ascites, fluid in the chest and generalized pitting edema. Accordingly, one can make a fairly good story for pneumococcal infection somewhere, leading to nephrosis and ending with a gradual "petering-out." It is too bad that we do not know

whether there were pneumococci in the culture. The fourth condition is acute glomerulonephritis. That was apparently considered also by the person who took care of the patient. I think we can rule it out. There were no red cells in the urine, and the rest of the picture was not particularly characteristic. Then one comes to the question, Did she have a cardiac condition? In favor of that was the enlarged liver. She had a certain amount of edema, a gallop rhythm and a fall in blood pressure, and one wonders if she had massive pulmonary infarcts, with a failing right ventricle. She did have right-axis deviation at one stage, but I do not believe that she had massive pulmonary emboli. There was no particular etiology for cardiac disease. She might have had pericarditis as the cause of the electrocardiographic changes, but that was probably not the diagnosis. The electrocardiographic changes can be explained by the edema of the skin, and do not necessarily indicate cardiac disease. I shall say that the patient did not have, primarily, cardiac disease. I do not believe they would have given the case to me if she had had. One of the more probable diagnoses is a hepatitis of some kind. People do get liver disease after pregnancy. She did have an expanding liver, and a peculiar mass on the right (?) side. She had a low serum protein, which would go with it, and a strange sort of exit, which does not show on the chart. She died with a fairly normal-looking chart, as so many patients with severe liver disease do, but the serum van den Bergh was not impressive, nor was there enough bilirubinuria for hepatitis. I do not believe that she died of toxic hepatitis. That is a diagnosis one might consider more seriously, however. The ecchymosis may have been indicative of vitamin K deficiency and severe liver disease.

The one diagnosis I really am hoping it may turn out to be is terribly far fetched. We know that patients who have severe hemorrhages at the time of delivery and who go into shock are prone to develop infarcts of the pituitary glands and resulting Simmonds's cachexia. We have had three such patients in the Ovarian Dysfunction Clinic. Could this patient have had this? From her red-cell count, it is apparent that she lost a large amount of blood at the time of delivery, following which she ran a rapidly downhill course. The blood chemical findings were quite extraordinary, and I think more attention should have been paid to them in the treatment. Both the serum chloride and the serum carbon dioxide combining power were lowered, each by about 10 milliequiv. per liter. Since these are both anions,

and since the sum of the anions in the serum equals the sum of the cations, we can infer either that the patient had an accumulation of some other anions in her serum or else that her cations were correspondingly low. The most likely possibility is that she had a low serum sodium. This would suggest an adrenal insufficiency or possibly adrenal insufficiency secondary to pituitary disease, that is, Simmonds's cachexia. Of course, the high nonprotein nitrogen and the high uric acid fit in with acute adrenal failure. Against the diagnosis of pituitary infarct, of course, is the general anasarca. I never heard of a patient with Addison's disease or Simmonds's disease who had general anasarca.

In conclusion, if the patient has any endocrine disease, I believe it is Simmonds's cachexia, with a terminal urinary infection. My second choice is liver disease. My third choice is pneumococcal infection with nephrosis.

DR. MALLORY: Are there any other suggestions?

DR. PAUL D. WHITE: May I say a word about the electrocardiogram? I think it is unlikely that edema alone would have such a preponderant influence on the T waves. It may have a striking influence on the total voltage of both QRS and T waves, but there are possible factors behind the edema such as renal or adrenal insufficiency that could change the T waves to this degree without necessarily any intrinsic heart disease or blaming the anasarca. What do you think, Dr. Sprague?

DR. HOWARD B. SPRAGUE: I wondered why the right-axis deviation developed.

DR. WHITE: That was only on the first occasion and was slight.

#### CLINICAL DIAGNOSIS

Acute glomerular nephritis with edema.

#### DR. ALBRIGHT'S DIAGNOSES

Pituitary infarct, with Simmonds's cachexia.  
Terminal urinary infection.

#### ANATOMICAL DIAGNOSES

Acute pyelonephritis.  
Nephrosis?  
Thrombophlebitis of uterine veins.  
Multiple pulmonary infarcts.  
Septic thrombosis of right auricle.  
Anasarca.

#### PATHOLOGICAL DISCUSSION

DR. MALLORY: Dr. Albright is safe in one regard, I am sorry to say, because the pituitary

gland was not examined, so that I can rule Simmonds's disease neither in nor out. We did, however, find a good deal wrong in various other organs. The most striking lesions were in the kidneys, which were considerably enlarged, and contained multiple small abscesses especially numerous in the left kidney. The pelvis of the left kidney was inflamed, and there was also a severe hemorrhagic cystitis. The question might be raised whether it was a hematogenous infection or a retrograde infection. I should say that it was definitely hematogenous, but the process still lies within the group of processes that we lump together as pyelonephritis. The theory of retrograde infection has rather disappeared in recent years, and we consider the vast majority of these cases to be hematogenous. The next question to come up is whether there was anything besides pyelonephritis. The glomeruli were perfectly normal. The tubules showed a very distinct swelling of the tubular epithelium and the presence of enlarged albuminous granules. The picture is not much beyond what is ordinarily called cloudy swelling, which may be found as the terminal stage of many febrile illnesses, but on the other hand, it is perhaps just a little bit beyond it and one might be justified in suspecting a nephrosis. If so, it was considerably masked by the severe pyelonephritis.

The right auricle contained a thrombus that appeared septic, both grossly and microscopically. The condition could be called, I think, an auricular endocarditis if one wished. The direct smears and cultures, however, failed to show organisms or growth. Thrombi in the uterine veins also suggested sepsis. There was massive edema, and each pleural cavity contained over a liter of fluid. There was 150 cc. of fluid in the pericardium.

The abdomen contained considerable ascitic fluid. The liver was not enlarged, weighing only 1300 gm., and this again is an example of a rather small liver readily felt in a patient who has ascites.

DR. WHITE: Was the pleural fluid clear?

DR. MALLORY: Yes; the lungs were also very wet.

DR. WHITE: Did the myocardium show any involvement?

DR. MALLORY: Not that of the ventricles. Beneath the septic thrombus in the auricle, there was some inflammation.

A PHYSICIAN: What was the mass described in the clinical findings?

DR. MALLORY: It may have been the gall bladder, the wall of which was edematous and thickened. Nothing else was found to account for it.

DR. ALBRIGHT: What was the cause of death?

DR. MALLORY: I think it is difficult to be sure of the mechanism of death. I should be inclined to think it was respiratory embarrassment from large amounts of pleural fluid and pulmonary edema. The patient certainly had infection too, but cyanosis was spoken of repeatedly in the course of the record.

DR. BERNARD M. JACOBSON: Do you think it was a fairly acute pyelonephritis coming on a few weeks before delivery?

DR. MALLORY: I should have to guess from the autopsy findings that the pyelonephritis was the chief cause of death. I cannot rule out the possibility of some degree of nephrosis as well, but I should like to make one diagnosis, and that would be pyelonephritis.

DR. ROBERT E. GLENDY: Were there abscesses in any of the other organs?

DR. MALLORY: No.

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## THE ROSE OF NO MAN'S LAND

FOR two years, we have been told how different this war is, but as we prepare to defend ourselves and as we watch the British facing its realities, we realize that some of the alleged differences have been purely imaginary. One of the most wishful thoughts has been that man power would not be needed—that this was to be a war of machines. In certain branches, this may be partly so, but in the medical services it is not. One after another, we see the familiar lacks and inadequacies facing us again. It makes little difference whether a man is wounded on a battlefield or in a wheat field or at his desk or in his bed—he must be the recipient of the very best medical and surgical care that can be devised under the circumstances. Preserved blood and serums may replace gum

acacia and salt solutions, and tetanus toxoids may replace antitoxins, but medical and surgical services will be more than ever in demand.

It is thus not surprising that the nurse—dramatized in the other war as the “rose of no man's land”—is again coming into such demand that she must soon be vigorously recruited if our national supply is not to fail us in the coming crises. Fifty thousand well-educated young women have already been called for by the Surgeon General of the United States Public Health Service to avert “serious damage to the Nation's health during the present emergency.” These young women, by entering the already established schools of nursing in our civilian hospitals,—particularly if they are well educated,—can soon relieve staff nurses who are already fully trained and who are already in demand, at least for the nurse-corps reserves of the United States Army and Navy.

In addition to enrolling approximately 600 reserve nurses per month, the Army at the present time has nearly 6000 nurses on active duty and anticipates an authorized quota of 8237 nurses for the fiscal year of 1942. The Surgeon General of the Navy has stated: “The Navy Nurse Corps has now approximately 700 nurses on active duty, including nearly 140 reserve nurses. There are more than 1000 reserve nurses awaiting a call to duty, and this number may be increased by an additional thousand or more by the end of the year.” Practically all such nurses must come from those now in civilian nursing duties, and it can accordingly be seen just where the shoe is going to pinch.

If we are to keep abreast of military and civilian nursing requirements, these 50,000 young women must be enrolled for the fall term in accredited schools of nursing. Surgeon General Parran has stated, “An especial effort should be made to enlist the interest of young college women in this important field, inasmuch as the greatest demand is for nurses who have had a superior education.” Under Dr. Parran's direction, the States Relations Division of the United States Public Health Service is administering a recent congressional appropriation of \$1,250,000, which will facilitate the

training of additional nurses, presumably in the schools of nursing already established and accredited

Even more than in the last war, young women as well as young men are actively challenged. Again, we begin to visualize some of the difficulties to be faced by those who will be charged with keeping "the home fires burning," for the depletion of our civilian nursing services is inevitable. Energetic action to recruit nurse trainees on an emergency and patriotic basis is in order now. If the use of machines—x ray, electrocardiographic and so forth—is doubled in the medical and surgical services of this war, the use of man power and woman power must be tripled.

### SALVATION ARMY APPEAL

THE Greater Boston Annual Maintenance Appeal of the Salvation Army will begin on September 16 with a dinner at the New England Conservatory of Music. Scores of volunteer leaders and workers will assist in raising the \$200,000 that is the goal for 1941-1942.

In the corps cities of Cambridge, Chelsea, Everett, Malden, Medford and Somerville, separate campaigns will be directed to collect the amount set for this year. The quota assigned to the thirty-two towns in which the Salvation Army does not conduct corps organizations is \$40,000.

The Salvation Army, which maintains more than thirty institutions that care for the needy, merits the support of all members of the community. It is hoped that physicians in particular will respond generously, as they have in previous years, to this appeal for help.

### MEDICAL EPONYM

#### KAHN TEST

The precipitation test for syphilis that has attained the widest use in this country is that proposed by R. L. Kahn (b 1887), of the Michigan Department of Health, in his paper, "Simple Quantitative Precipitation Reaction for Syphilis," which appeared in the *Archives of Dermatology*

and *Syphilology* (5: 570-578, 1922). The author's test has been modified and discussion of it amplified in numerous later papers and a book.

The precipitation method proposed in this paper is based on the employment of syphilitic serum with alcoholic extract anogens of heart muscle. In this regard it is similar to the precipitation reactions of Meinicke, Sachs and Georgi, and Dreyer and Ward.

The test proposed, however, differs from each of these reactions in essential phases.

R W B

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

#### INDUCED ABORTION, FOLLOWED BY FATAL HEMORRHAGE AND SEPSIS

A thirty-nine-year-old primipara arrived in the hospital flowing profusely and evidently septic. She stated that her last period had occurred approximately four months before admission, and that an abortion had been induced. The previous medical history was irrelevant.

The patient's temperature was elevated, but the record does not state how high it was. Physical examination was negative except for an abdominal tumor mass, which rose above the symphysis and was consistent with the size of a four-months' pregnancy. One foot was protruding from the introitus. Under aseptic precautions, the fetus was extracted and the uterus curetted of retained placenta tissue. The record suggests that a large part of the placenta was lying over the internal os, and when this was removed, a tremendous amount of blood followed. The patient went into extreme shock, and was given ergot, pituitrin and stimulants. The vagina and uterus were tightly packed with gauze, and the patient was returned to bed. She died shortly thereafter.

*Comment.* It is well recognized that artificial emptying of the uterus during the second trimester is very difficult, and that hemorrhage and sepsis frequently follow an attempt to induce such evacuation. This case is said to have been self-induced; at any rate, both sepsis and hemorrhage followed. No transfusion was given, and it is doubtful whether it would have been of any value, because the hemorrhage from a uterus at this period of gestation may be perfectly tremendous. There is little in the history to criticize. It is sad.

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, Secretary, 330 Dartmouth Street, Boston.

that the operation lasted twenty minutes. If the bleeding had continued from the first at a startling rate, it would have been more conservative to pack the uterus and permit some of the placenta to remain, rather than to continue the operation with the idea that the uterus must be emptied. This is the cardinal treatment of any criminal abortion. In the face of very active hemorrhage, all attempts to remove the products of conception should be postponed, the immediate hemorrhage should be treated by uterine packing, and the patient should be transfused while still alive.

## DEATHS

BARNES — J. ARTHUR BARNES, M.D., of Worcester, died September 6. He was in his seventieth year.

A native of Fitchburg, Dr. Barnes received his degree from Harvard Medical School in 1900. He was a fellow of the American College of Surgeons, the Massachusetts Medical Society and the American Medical Association.

He is survived by his widow, a son, a brother and a sister.

STONE — FRANK E. STONE, M.D., of Lynn, died September 3. He was in his eightieth year.

Born in Lynn, Dr. Stone received his degree from Bowdoin Medical School in 1885. He was a member of the Massachusetts Medical Society and the American Medical Association. He was on the staffs of the Lynn and Union hospitals.

His widow, a son, two daughters and a sister survive him.

## MISCELLANY

### TUBERCULIN TESTING IN CHICAGO SCHOOLS

Findings in an extensive tuberculosis survey in Chicago schools, using the tuberculin test as a screen, are now available (*City of Chicago Municipal Tuberculosis Sanitarium Bulletin*, 18 [1938], 19 [1939] and 20 [1940]). Although it is not a new conclusion that routine skin testing in elementary-school groups is not an economical procedure, the report does contribute materially to knowledge of the epidemiology of tuberculosis and permits comparison with previous surveys in Chicago. An abstract follows:

This survey was carried out by the Chicago Municipal Sanitarium, aided by the Tuberculosis Institute of Chicago and Cook County.

The survey policy of the Municipal Tuberculosis Sanitarium had hitherto been largely oriented toward older groups. Tuberculin testing in the schools, therefore, represented a deviation from established policy and was undertaken to explore educational values, morbidity rates, and case-finding potentialities of a follow-up of the reactors and to check on existent case-finding machinery.

Since the purpose was to obtain a cross-section of tuberculosis morbidity, the survey attempted to include every Chicago school. However, it was necessary to sacrifice certain ambitions, such as a 100 per cent consent and a

thorough survey of each school. In a general way, the policy ran, "Get what consents you can in the time allotted and go on to the next school."

Kindergarten children, those in the first and eighth grades and all available students in the high schools, were examined. It was thought that a positive reaction in a kindergarten or first-grade child might have some epidemiologic significance. Eighth-grade children, on the threshold of adolescence, were included because many would not go to high school; thus it might have been the last chance to include them in a case-finding effort. In view of the many studies already made, the justifiability of high-school examination is hardly debatable.

First, the Board of Education notified the principals. Then the nurse addressed the teachers and children in each room. All were given appropriate literature, which, with the consent card, the children took home. After a proper interval, a team did the tuberculin test, and the results were read in forty-eight hours.

In all, 176,878 consents were obtained in 561 public elementary schools, 115 public high schools, 347 parochial elementary schools, 47 parochial high schools, 12 trade and vocational schools and 5 junior colleges.

A self-contained and complete mobile unit, the first known to be used in the x-ray field, was devised. On starting work the truck drove into the schoolyard and the technician selected a location as near as possible to space for extra dressing rooms. Current was obtained through a cable from a school connection.

The procedure, carefully standardized, was to give a single Mantoux test, using PPD (purified protein derivative) in an amount one tenth the usual final dose. The percentage of reactors with this dose was low compared with the experience in other urban areas, so that the dose was doubled in the latter part of the work, except with Negroes and Mexicans, who had shown marked sensitivity to tuberculin.

In the 167,345 children tested, 27,401 proved positive. To March 1, 1940, 23,532 had been x-rayed and 218 cases of reinfection-type tuberculosis had been found, of which 109, or 50 per cent, were in the moderately or far-advanced stage; in 4524 children, evidence of primary-infection-type tuberculosis was found.

The reactor rate and the primary tuberculosis rate were practically the same for boys and girls, but the incidence of reinfection-type tuberculosis was twice as high in girls. The incidence of disease among children x-rayed was higher in Negroes and Mexicans but not to the same degree as the infection rate. The Negroes had slightly less primary tuberculosis than the Whites.

The study seemed to bear out the reports of other workers who found a lack of constant correlation between tuberculin sensitivity and tuberculous calcifications.

In comparison with other metropolitan surveys, the reaction incidence in Chicago is low. This may be because no person with an open case may live in the same home with children under sixteen: contact is broken as soon as possible after discovery of the case.

Survey results confined to a district or a constellation of districts would lead to false conclusions. The survey included schools in every district and children from every economic level. The major part of the tuberculosis problem is sharply localized. About four of the seventy-five census districts account for 38 per cent of the deaths. Mortality in these areas is much higher than the general rate, namely, 196 per 100,000, as compared with 51.6 per 100,000 for the city as a whole; morbidity figures also run in the same ratio.



In Chicago, as elsewhere, decreasing mortality rates probably exerted an influence on the composition of the infection index. The rate has fallen from 147.9 per 100, 000 in 1917 to 51.6 in 1939. Over the same period, the rate has fallen from 133.9 to 34.0 for Whites and from 144.0 to 281.7 for Negroes.

In an attempt to estimate the diminution of the reactor rate, the present figures may be compared to older studies, one made by Webb of the University of Chicago in 1930-31, and the other by Novak and Kruglick of the Tuberculosis Institute of Chicago and Cook County in 1933-37. Webb tested no high school children, and Novak and Kruglick tested no elementary school children. In elementary school ages, comparing Webb's figures with the present study, since 1930-31 there has been a definite drop for each age period. Comparing high school tests for 1933-37 and 1936-39, there has also been a substantial drop for each age period, except for age twenty, only 29 students of this age were tested in the Novak study.

The specific relation between tuberculin positive reactors and tuberculosis in the home was clearly demonstrated in the present survey. The source of infection was unmistakably established in 3284 cases, but of these only 226 were new pulmonary cases.

The comparatively small number of new cases found in the families of the positive reactors was both a disappointment and a satisfaction. A larger proportion of new tuberculosis had been anticipated, but it was encouraging to know that the existent case-finding machinery is effective, since in 90 per cent of the cases the source of infection was already under supervision.

Altogether, 586 new cases of tuberculosis were found. The total cost chargeable to the survey for the 586 cases found was \$511.95 per case.

To explore its potentialities, figuratively speaking, the miniature x-ray machine was carried almost to the door step of the people in the congested areas. The equipment was hooked up to the mobile x-ray truck, and this self-contained unit, including dressing rooms, was taken to various locations.

The plan, still operative, aims at making an x-ray examination of every man, woman and child in certain areas of gross congestion, high tuberculosis mortality and low economic status.

In the school survey, lasting three years and comprising 23,532 x-ray examinations, 218 new cases were found on the first film. In the miniature x-ray survey, comprising 20,956 examinations and lasting five months, 675 new cases were found by the original x-ray film.

To summarize, during a three-year period, 167,345 children were tuberculin tested, and 23,532 x-rayed. The reactor incidence was 7.04 per cent for kindergarten and first grade, 18.82 per cent for eighth grade, 21.29 per cent for high school students and 29.97 per cent for miscellaneous schools and colleges. The rate for Negroes was twice that of Whites, and for Mexicans it was still higher.

The study showed a substantial drop in the reactor rate in Chicago as compared with older studies. The city-wide survey emphasized the fact that each district had its own reactor rate, which was allied to local mortality rates.

In 57,481 children under twelve tested with tuberculin, 9 cases of pulmonary disease were found, which is comparable with figures for this age group in the mortality tables. Facts point toward the adolescent and early adult years as the case-finding provinces. In testing adults in highly infected milieus (60 per cent reactions or more), x-ray study of the entire group is cheaper than tuberculin

testing, with x-ray examination of the positive reactors — Reprinted, in part, from *Tuberculosis Abstracts*, August, 1941

## HARVARD MEDICAL SCHOOL

Award of sixty-five Harvard Medical School scholarships totaling \$21,295, for study during the 1941-42 academic year, has been announced by Harvard University. The recipients of the scholarships are:

Chuan Wang, 1M, Hong Kong, China, Harold S. Robinson, 3M, Shantung, China, Robin G. Anderson, 2M, Passaic, New Jersey, Harold Brown, 2M, Dorchester, Massachusetts, Theodore G. Erler, Jr., 3M, Bellevue, Ohio, William J. Lahey, 3M, East Hartford, Connecticut, Sidney W. Ellery, 2M, Miami, Arizona, Elliot L. Sagall, 2M, Revere, Massachusetts, Grant V. Rodkey, 2M, Coeur d'Alene, Idaho, William Rudder, 1M, Bellingham, Washington, Thomas D. Allison, 2M, Kittanning, Pennsylvania, Robert L. Berg, 1M, Spokane, Washington, Logan O. Jones, 2M, Birmingham, Michigan.

James M. Judd, 1M, Randolph Center, Vermont, Frank E. Trobaugh, Jr., 1M, West Frankfort, Illinois, Duane H. Mitchell, 2M, Winchester, Kansas, John A. Evert, Jr., 3M, Glendive, Montana, Jesse E. Thompson, 2M, San Benito, Texas, Alvin T. Held, 4C, Columbus, Ohio, Paul A. Reinenschneider, Cleveland, Ohio, Bernard W. Robinson, Roxbury, Massachusetts, Boris P. Bushueff, 1M, Harbin, Manchou T'iao, William R. Waddell, 1M, Tucson, Arizona, James E. Kreisler, 3M, Austin, Texas, Lindley B. Reagan, 3M, Poughkeepsie, New York, David W. Williams, 2M, Washington, Connecticut.

Francis R. Lane, 1M, Somerville, Massachusetts, Richard J. Cundiff, 2M, Long Beach, California, John Q. U. Thompson, 3M, Jacksonville, Florida, Edwin W. Peterson, 1M, Denver, Colorado, David S. Speer, 2M, Bronxville, New York, James H. Strough, 3M, Canton, Ohio, Herbert R. Morgan, 3M, Bell, California, Harold F. Searles, 1M, Hancock, New York, Israel H. Schleinberg, 1M, New York, New York, Stephen L. Midey, 1M, Buffalo, New York, Harry D. L. Kaye, 3M, New York, New York, Daniel Scarra, 1M, Paterson, New Jersey, Burdick G. Clarke, 3M, Winnetka, Illinois, James P. Dixon, Jr., 1M, North Rochester, New Hampshire, Charles Averill, 3M, Methuen, Massachusetts, Theodore S. Cobbe, Jr., 1M, Canton, Ohio.

Abraham N. Barger, 2M, Greenfield, Massachusetts, Melvin B. Black, 1M, Roxbury, Massachusetts, James T. Blodgett, 3M, Woburn, Massachusetts, Frederic B. Breed, 2M, Cambridge, Massachusetts, Donald E. Brown, 2M, Beverly, Massachusetts, Robert H. Brown, 1M, Hyde Park, Massachusetts, John Burbank, 2M, Lynn, Massachusetts, Allan D. Callow, 3M, West Somerville, Massachusetts, Dante F. Campagna Pinto, 2M, Boston, Massachusetts, David Dove, 3M, South Sudbury, Massachusetts, Robert W. Gage, 3M, Needham, Massachusetts, Thomas V. Healey, 1M, Worcester, Massachusetts, Robert B. Higgins, Cambridge, Massachusetts.

Robert B. Holden, 2M, Stoneham, Massachusetts, Elmer V. Kennally, 1M, Medford, Massachusetts, Eugene F. Poutasse, 1M, Weston, Massachusetts, Cornelius J. Shea, 2M, Dorchester, Massachusetts, Robert J. Tracy, 3M, Concord, Massachusetts, Paul F. Ware, 2M, Clinton, Massachusetts, Eugene L. Watkins, 1M, Worcester, Massachusetts, Albert E. Weiner, 3M, Newton, Massachusetts, Mark S. Wellington, 1M, Amherst, Massachusetts, and Frank C. Wheelock, Jr., 2M, Springfield, Massachusetts.

## CORRESPONDENCE

## SULFANILAMIDE SPRAY

In a letter published in the November 14, 1940, issue of the *Journal*, one of us (N. C. S.) suggested the use of a sulfanilamide spray in the treatment of colds and sore throats. Its local application in infected wounds has been used with considerable success, and it seemed reasonable to think that it would have a similar effect on inflamed throats and infected nasal passages.

Three 5-gr. tablets of sulfanilamide are dissolved in an ounce (30 cc.) of hot water. The tablets go into solution better if they are finely pulverized; however, even then, a sediment remains, which is liable to clog the atomizer. Sulfathiazole goes into solution better than sulfanilamide and appears to be equally effective, although our experience with it has been limited. When one is using sulfathiazole, two 7½-gr. tablets are dissolved in an ounce (30 cc.) of hot water.

We are convinced that the effects of the spray are markedly beneficial. The majority of colds and sore throats clear up in about half the time of the usual duration. It probably has no effect on the virus that causes the cold, but is markedly effective against the secondary invaders, and the earlier the cold is treated the better chance there is of holding the latter in check.

Colds that begin with inflamed throats give the most spectacular response. In a few hours, the redness fades, and the soreness disappears. A streptococcal sore throat rarely persists over twenty-four hours.

Since January, 1941, the beginning of the winter term, we have used the spray in the treatment of colds among the students of the Putney School. The days lost because of colds in the fall, winter and spring terms, compared with those of the two preceding years, are as follows:

1938-1939 (112 pupils).	Fall term	94 days
	Winter term	104 days
	Spring term	19 days
1939-1940 (122 pupils).	Fall term	180 days
	Winter term	128 days
	Spring term..	39 days
1940-1941 (136 pupils).	Fall term	104 days
	Winter term	89 days
	Spring term	13 days

During 1940-1941, we had the best health record of any year since the founding of the school in 1934. Although we were in the midst of a severe epidemic of influenza, no serious illness occurred. There were only two cases of influenza, no cases of pneumonia, and no cases of bronchitis, which had been particularly bothersome in other years. There were a few cases of earache, but none that required paracentesis.

We do not mean to give the impression that the sulfanilamide spray was responsible for the small amount of illness, although we believe it was effective in stopping the invasion of tissues by secondary invaders, which in some cases ultimately result in sinusitis, bronchitis, pneumonia and otitis media. Furthermore, we believe it somewhat limits the contagiousness of colds.

At the Putney School, every child is inspected every day, and the slightest sign of a cold is treated immediately with the sulfanilamide spray. The treatment is continued every two or three hours for forty-eight hours, or until the cold has cleared up.

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## REPORT OF MEETING

## NEW ENGLAND PATHOLOGICAL SOCIETY

A regular meeting of the New England Pathological Society was held on May 17 at the Yale University School of Medicine, New Haven. Dr. Tracy B. Mallory presided.

The first paper, on "Wernicke's Hemorrhagic Polioencephalitis," was presented by Drs. J. P. Murphy, C. O. Prickett, A. J. Waring, Jr., and H. M. Zimmerman. Employing an experimental dietary regime in which thiamin and nicotinic acid were withheld or were given in small quantities, the authors reinvestigated the problem of the etiology of Wernicke's disease, with the rat as the experimental subject. All the other vitamins were given in amounts known or estimated to be adequate for this animal. Four groups of animals were used, and in the brains of those which received no vitamin B<sub>1</sub>, or minimal amounts of it, the typical hemorrhagic and angioneurotic vascular lesions were found in the gray matter around the third and fourth ventricles and aqueduct of Sylvius. The nuclei of the vestibular nerves and of the cerebellum particularly were frequently and severely involved. The pathological findings were just as extensive when nicotinic acid was fed to the hypothiaminotic animals as when it was absent from the diet. From these studies, the investigators concluded that uncomplicated thiamin deficiency in the rat results in the production of lesions typical of Wernicke's disease; that concomitant deficiency in nicotinic acid does not significantly increase the number and extent of the lesions; that deficiency in nicotinic acid alone does not result in these changes; and that the longer the length of life of the animals not receiving B<sub>1</sub>, the severer and more extensive the polioencephalitic changes tend to become. In the discussion, Dr. M. C. Winternitz asked whether it is known how the thiamin hydrochloride deficiency produces these changes. Dr. Zimmerman answered that thiamin hydrochloride has something to do with the metabolism of carbohydrate, and it is quite possible that its effect is similar to that produced by the deprivation of glycogen and glucose. It may, of course, have something to do with oxygenation in the central nervous system, producing anoxic effects. He also noted that lesions of this kind due to vitamin B<sub>1</sub> deficiency have been seen in four species—the pigeon, rat, dog and man. Similar lesions are seen in man in the absence of alcohol, and the symptoms of those patients afflicted with Wernicke's syndrome are ameliorated by adequate amounts of thiamin hydrochloride.

The second paper, "Factors in Resistance to Tuberculosis," was presented by Drs. Bruno Gerstl and Robert Tennant. From the variance in response to the tubercle phosphate when injected into rabbits or mice (Sabin, Thomas), it was concluded that the mouse cells are able to break down rapidly the tubercle lipid, and that those of the rabbit do it at a slower pace, if at all. This ability of the mouse cells may be one of the additional factors on which the natural high resistance of the mouse to tuberculosis is based. It could be demonstrated that phosphatases alone were not able to break down the tubercle phosphate. The previous action of a second enzyme, a lipase in a general sense, was necessary. Lecithinase "A" obtained from snake venom was one of the particular lipases facilitating further splitting; it could not be ascertained, however, in the parenchymatous organs of the mouse. Another lipid-splitting enzyme was obtained from the mouse liver and differentiated from other esterases by using quinine as an inhibitor. Its action, com-

bined with that of phosphatases, effected 80 to 90 per cent splitting of tubercle phosphatide or lecithin, whereas either enzyme alone accomplished little. Comparison of the reaction velocities of phosphatases of the three species, mouse, rabbit and guinea pig, showed marked differences. When the tubercle phosphatide was used as substrate, the mouse enzymes produced a rapidly progressing cleavage, the guinea pig lung, none at all, the effect of the rabbit organs was in between. Experiments in progress suggest that this difference is due not only to variations in enzyme concentrations but also to the inhibition exerted by the tuberculostearic acid split off from the phosphatide. This inhibition varies with the species from which the enzymes are derived. The discussion was opened by Dr. Valy Menkin, who stated that, a number of years ago (1928, 1929), Lurie, of the Henry Phipps Institute, demonstrated that rabbits infected with tubercle bacilli displayed differential destructive capacity in various organs. The bacilli were rapidly disposed of by the spleen, liver and bone marrow while, on the other hand, these micro-organisms persisted in the lungs and kidneys. There has been no adequate explanation offered for this difference in local organ immunity. Dr. Menkin wondered whether the findings of Dr. Gerstl on the splitting and liberation of phosphorus compounds could not yield a clue to this fundamental problem. In other words, is it possible that these same organs would yield differences in chemical activity that could in turn be correlated with the number of recoverable bacilli in the respective organs? He considered this to be of definite interest, since the speaker's thesis was apparently designed to show that some of the factors of resistance in tuberculosis are to some extent associated with the ability of tissues to split phosphatide compounds. He was not certain whether or not the last chart shown suggested the possible existence of any such quantitative correlation in the organs studied. Dr. Gerstl replied that Corper, in 1931, also demonstrated that canine lungs, liver and spleen are able to destroy tubercle bacilli when incubated for several weeks. The charts shown indicated that there is a difference in the rate of splitting the tubercle phosphatide when organ extracts of the same species—and, still more, when organ extracts of the mouse, rabbit and guinea pig—are compared. This ultimately results in a quantitative difference. These investigations differ from those first mentioned by the employment of purified extracts and by the attempt to determine the enzymes responsible for the breakdown of the tubercle phosphatide.

The third paper, "Experimental Brain Tumors Produced with Benzpyrene," was presented by Drs. H. Arnold and H. M. Zimmerman. Attempts at producing cerebral neoplasms with benzpyrene have in the past yielded uniformly negative results. In most of these experiments, the carcinogen was administered in an oily vehicle such as lard, cholesterol and lanolin, and only granulomatous reactions were produced at the sites of benzpyrene implantation. In the present experiment, 51 mice of the C-3H strain had pellets of the pure carcinogen implanted in the right cerebral hemisphere. Up to the three hundred and twenty-fourth day of the experiment, 27 of the animals died or were killed, and of these, 22 had intracranial neoplasms. Eleven were gliomas, 10 were sarcomas, and 1 was a mixed tumor of gliogenous and sarcomatous origin. Included among the gliomas were 3 glioblastomas multiforme, 1 oligodendroglioma, 1 astrocytoma, 3 ependymoblastomas, 1 medulloblastoma and 3 unclassifiable gliomas. Most of the tumors have been transplanted successfully in the subcutaneous tissues of other mice of the same strain. It has been found that the tumor transplants are of great value in the classification

of the experimental neoplasms because typical morphologic features, absent in the original tumors, frequently appear in the second and third hosts. In the discussion, Dr. Zimmerman stated that it is interesting to speculate on the reasons why previous benzpyrene experiments to produce intracranial neoplasms were unsuccessful. Perhaps the wrong animal was used, or, more probably, the carcinogen was inserted in the wrong vehicle. It is quite possible that the granulomatous change that may have been produced was too great, and killed the animal before the tumor developed. It is also interesting to speculate on how the carcinogen acts. Is it merely a catalyst? Since gliomas practically never metastasize outside the brain, it was believed that there must be some antagonism to the growth of ectodermal gliomas on the part of mesodermal tissue. The fact that these tumors have been successfully transplanted in subcutaneous tissue proves that there is no local antagonism. Dr. Mallory mentioned that he had seen a malignant teratoma of the ovary containing glial tissue, with omental implants of the glial tissue, and asked whether any of the mixed tumors had appeared in the transplant as mixed tumors. Dr. Zimmerman answered that it is possible to get mixed tumors in the transplant. On the other hand, transplantation of the mixed tumors is one method of separating them. One of the transplants may yield a glioma, and the other a sarcoma, a process quite analogous to the isolation of bacteriologic colonies.

The next four papers dealt with kidney and cardiovascular disease. The general survey of the experimental approach was presented by Dr. M. C. Winternitz. The results of bilateral nephrectomy in the dog have been found to contrast sharply in various ways with those following ligation of both main renal arteries. This has been pointed out for the blood pressure, which does not usually rise and never attains significant proportions after ablation of both kidneys, but which, as a rule, does become elevated after ligation of both renal arteries. Other contrasts, thus far not emphasized, involve survival time, rate of rise of blood nonprotein nitrogen, quantitative change of electrolytes of the blood with associated effects on cardiac function and, finally, the ultimate contrasting morphologic processes manifested after the two procedures. Moreover, the bilaterally nephrectomized animals have proved valuable for determination of the acute functional and structural effects caused by the injection of whole extracts and also of fractions of extracts of kidney and other organs of homologous and heterologous species. The results of these experiments have encouraged the utilization of similar extracts with normal dogs, and chronic counterparts of the acute processes are now being obtained. Dogs survive bilateral nephrectomy as long as ten days, the average is seven, and very few die before the end of the fifth day. The blood pressure shows little change. Vomiting occurs almost invariably. At autopsy, no specific gross lesions are encountered. Occasional sub-endothelial, valvular and visceral hemorrhages, as well as focal necroses involving heart muscle and smooth muscle of artery wall, alimentary or genitourinary canal, are rare but important findings. Ligation of the main renal artery of both kidneys may result in a moderate but definite rise in the blood pressure, which tends to fall again on the last day of survival of the animal. The nonprotein nitrogen of the blood rises rapidly, and by the third postoperative day equals that of the sixth day after bilateral nephrectomy. Vomiting is a prominent feature of the short clinical course. The animals give evidence of serious illness rather suddenly during the latter part of the second postoperative day and then become progressively ill, with signs of central nervous-system irritation, includ-

ing nystagmus and, rarely, convulsions. The short survival period contrasts sharply with that of the nephrectomized animal. Death has occurred after ligation of both renal arteries not later than the fourth postoperative day, whereas animals whose kidneys have been removed often live twice, rarely three times, as long. The gross post-mortem examination shows hemorrhagic lesions of wide distribution similar to those described as following much longer periods of hypertension and azotemia after constriction of the renal arteries. Edema, hemorrhage and necrosis of muscle, including heart muscle, smooth muscle of blood-vessel walls, hollow viscera and diaphragmatic muscle, are the lesions encountered. It should be emphasized that a minimal representation of the extensive anatomic changes found after ligation of both main renal arteries may be demonstrated by detailed examination when death follows removal of the kidneys. Consequently, absorption from the necrotic kidneys cannot be considered the only responsible factor. After ligation of both ureters, the lesions encountered, except for those of the kidney, conform to those that result after ligation of both main renal arteries. The results of the injection of extracts of necrotic and of normal dog kidneys into the bilaterally nephrectomized dog are strikingly similar. The injection may be associated with a slow rise in blood pressure, which reaches a maximum only after several minutes and then falls very gradually over an even longer period before it drops to the preinjection level. Nystagmus, vomiting and occasional convulsions may occur, with or without fall in pressure. The blood nonprotein nitrogen of the injected animal has a tendency to rise abruptly, as that of the ligated animal does. This rise is not due to the nitrogen content of the injected protein. The anatomic changes duplicate those that follow ligation of both main renal arteries. Their extent is associated both with the survival time of the animal and with the amount of extract received. Crude extract of pig kidney, obtained by the Buchner press or the Latapie technique and injected into nephrectomized dogs, has the same effects as dog kidney extract. The depressor effect is more constant than with dog kidney preparations. Dialyzation does not deprive the extract of either its vasopressor or its dilator properties. Intravenous injection of tissue extracts, as is well known, exerts a profound effect on blood coagulation time and actual clot production. It should be emphasized that many of these effects are encountered after partial or complete renal arterial or ureteral occlusion and that they include both vasal depressor and pressor actions, changes in blood nonprotein nitrogen, and electrolytes, hemorrhage and necrosis of muscle, including both heart muscle and the smooth muscle of blood vessel walls, and hollow viscera particularly. These occur in various combinations, and the fact that at least some may be eliminated by particular treatments indicates their separate origin.

One aspect of this problem, "Electrolytes, Potassium in Particular, and Cardiovascular Renal Disease," was presented by Dr. S. H. Durlacher. The electrocardiographic findings in potassium poisoning are similar to those seen in experimental renal insufficiency produced in animals receiving a normal diet. The serum potassium reaches lethal levels following extirpation of the kidneys and bilateral ligation of the renal arteries or ureters. The survival time of rats fed a diet deficient in potassium with consequent diminution of muscle and serum potassium, is significantly increased following the above procedures over animals fed a control diet. The animals die after a prolonged period, with markedly elevated blood non-protein nitrogen. The serum potassium levels are not within the fatal range at the time of death. Hypertrophy

of the rat kidney, which occurs after a three-week period on a low potassium regime, consists in dilatation of the tubules of the medulla and pyramid, with hyperplasia of the lining epithelium.

Another aspect of the subject, "Tissue Extracts, Blood Coagulation and Associated Anatomical Changes," was presented by Dr. R. Katzenstein. The well-known effects of tissue extracts on the clotting time of the blood and the production of thrombi are related to their content of thromboplastic substance. This varies considerably with different tissues. Lesions of the wall of heart and blood vessels are not necessary for thrombosis. Moreover, such mural changes occur without superimposed thrombi if the stability of the blood from the standpoint of its coagulation is not advantageous. Location of thrombi after injection of tissue extracts indicates variation in the coagulation time of the blood in different parts of the vascular bed and suggests that different organs participate in effecting the balance of the coagulation time.

Finally, the "Contributions to Cardiovascular Renal Disease from the Biochemical Approach" was presented by Dr. E. Mylon. Renin, the pressor substance present in normal renal tissue, was shown either to be attached to or to be a small molecular protein that is not precipitated by centrifugation at speeds of 50,000 revolutions per minute. Purification of the material diminishes the angioneurotic activity, although a blood pressure rise of 30 mm. of mercury is produced when quantities equivalent to 1 gamma of nitrogen per kilo are administered. This pure product is free of all enzymatic action, in contrast to the less-refined "renin-C" of Page and his co-workers. The necessity of an intermediary product such as "angiotonin," produced by Page, is questioned in the light of previous experiments by Landis, Montgomery and Speckman, who showed that the pressor substance acted only in the presence of an intact sympathetic nervous system. The failure of renin to produce contraction of an isolated artery is therefore not surprising. The depressor activity of crude kidney extracts, as well as similar preparations of other organs, is related to the thromboplastic activity of these products. When clot formation is inhibited by heparinization or by the postinjection negative phase of blood clotting, only a slight fall in blood pressure occurs. Kidney extracts do not, therefore, possess a strong depressor substance, and the sharp and sustained fall in pressure observed following the injection of these materials is dependent on their thromboplastic action. In the discussion, Dr. Menkin referred to his observations made recently on some preliminary studies on the subject of shock. This was induced by utilizing the method described by Dr. Walter B. Cannon a number of years ago, which, in brief, consists in studying blood-pressure changes after severe injury induced in the thighs of cats by crushing the muscles. The blood pressure is measured by the usual technique of introducing into the carotid vessel a cannula connected to a mercury manometer. In his experience, almost immediately after the severe injury has been induced, there is a sharp drop in blood pressure, which is sustained throughout the period of the acute experiment. This may last one or two hours. Furthermore, it is of interest that in these animals the rate of blood coagulation seems to be hastened, as evidenced by the frequent necessity of washing clots from the carotid cannula, a state of affairs not observed in animals with uninjured tissues. In view of the very interesting observations of extracts of tissues favoring the formation of thrombi, Dr. Menkin wondered whether thromboplastic substances may not be constantly diffusing into the circulation from an area of extremely

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## IS THERE A COMMON DENOMINATOR IN SCLERODERMA, DERMATOMYOSITIS, DISSEMINATED LUPUS ERYTHEMATOSUS, THE LIBMAN-SACKS SYNDROME AND POLYARTERITIS NODOSA?\*

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**S**CLERODERMA, dermatomyositis, disseminated lupus erythematosus, the Libman-Sacks syndrome and polyarteritis nodosa constitute a group of diseases of unknown etiology that are apparently unrelated in their presenting clinical features. The widespread visceral involvement in each is obscured by certain dominating focal manifestations, which serve as the clinical basis for the differentiation of these syndromes from each other. Striking similarities, however, in the detailed pathology of these various conditions require evaluation for a possible relation or common denominator among them. This communication reports a case of scleroderma that presented visceral features common to other diseases in this group. The systemic symptoms and pathology of these syndromes are discussed to define their differences and to determine whether any common relation exists.

### CASE REPORT

A 51 year-old unmarried secretary was first admitted to the hospital for study on August 23, 1939, because of generalized pigmentation suggestive of Addison's disease. The present illness first became manifest in the fall of 1937, when she noted that on awaking in the morning there was marked numbness and coldness of both hands, especially the right. In the winter of 1937-1938, both hands on exposure to cold became painful and showed whitish blue discoloration. There was never any pain or numbness of the feet. In January 1938, a diagnosis of arthritis was made, and x-ray films of the hands were interpreted as showing arthritic changes. The patient lost 18 pounds on a reducing diet, and received two series of vaccine injections, each lasting approximately 3 months. She consulted another physician in the spring of 1939 because of persistent severe pain in the right hand hardness of the finger tips bilaterally and difficulty in typing. He doubted the diagnosis of arthritis, and believed that the patient had scleroderma. Because of a basal metabolic rate of -27 per cent, the patient was given

between 2 and 3 gr. of thyroid daily which she took regularly to the date of admission. She also received Brewer's yeast, belladonna and phenobarbital. Her finger tips became much softer, and she could type without difficulty. During the summer of 1939, her right wrist became very stiff and painful, and the fingers gradually contracted and became so stiff that she could not close her fist tightly. The patient had noticed that her skin darkened rapidly every summer but that throughout the last year her chest had remained tanned. During that winter the skin continued to darken and became very shiny. Her appetite and strength remained fairly good, and her weight before admission was 128 pounds. Two weeks before admission, she developed a slightly sore area at the base of the 5th metatarsal bone of the left foot, which a week later became infected and discharged pus.

The past history was not remarkable. The patient had always been in excellent health. She had typhoid fever 27 years before admission and a hysterectomy for fibroid uterus 19 years later. There was no history of scarlet fever or rheumatic fever. The system and family histories were noncontributory. She had used no tobacco or alcohol.

Physical examination revealed intensely tanned skin, the backs of the hands being almost negroid in appearance. The skin of the anterior chest was glistening brown and stretched very tightly over the underlying structures. The skin over the malar portion of the face was likewise very taut. On the backs of the hands palms and fingers, the skin and subcutaneous tissues were thick and brawny. In the mouth there appeared one small area that was suggestive of pigmentation. Hyperkeratotic plaques were abundant on the abdomen. The fundi and the thyroid gland were normal. The heart and lungs showed no abnormalities, the blood pressure was 114/74. Abdominal examination revealed no unusual findings, and the peripheral reflexes were equal and hyperactive. The fingers were tapering and cold, and neither hand could close completely. The right wrist was extremely painful to palpation and movement. The skin over the legs was normal in texture except for moderate brawny edema of the left leg, with slight pitting at the ankle. At the base of the 5th metatarsal on the left, there was a fairly well healed infection. The dorsalis-pedis pulsation was bilaterally palpable.

The laboratory data, in view of the subsequent course, were of considerable interest. Of two routine urine analyses, the highest specific gravity was 1.003, and the sediment on one occasion showed 2 red blood cells in thirty fields. The red-cell count was 3,930,000, with a hemo-

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globin of 11.6 gm. (80 per cent Sahli), and the white-cell count was 12,200, with 73 per cent polymorphonuclear cells (10 per cent band forms) and no eosinophilia. Blood chemical findings included a nonprotein nitrogen of 27 mg., a urea nitrogen of 11 mg., a sugar of 99 mg. and a cholesterol of 195 mg. per 100 cc. Total protein on admission was 7.1 gm., with albumin 3.7 gm. and globulin 3.4 gm. The blood-sodium level was 321 mg., and the chloride 295 mg. per 100 cc. The serologic findings were negative.

During the hospital stay of 7 days, the patient's oral temperature reached an average of 99.4°F. daily, with a pulse rate usually of 90, and respirations of 20. A diet with a calculated salt intake of 5 gm. daily was ordered, and an actual intake of 3.2 gm. was maintained after the 1st hospital day. During the first 4 days the fluid intake was high, and there was a diuresis averaging more than 3500 cc. daily, the total urinary chloride exceeding 4.65 gm. Thereafter, fluid intake and output fell to normal levels, and the total urinary chloride was 1.40 gm. The 24-hour urinary creatine varied from 89 to 35 mg., and the creatinine from 1013 to 486 mg. The blood pressure, taken at frequent intervals, showed a gradual decline, reading 95/60 on discharge. The wrist was treated with hot, Epsom salt soaks, and the subsiding infection of the foot with hot, boric acid compresses and elevation. Both regions improved rapidly. It was considered that the blood-pressure readings, the levels of sodium and chloride in the blood, and the normal 24-hour urinary chloride excretion on a diet fairly low in salt were sufficiently significant to eliminate the diagnosis of Addison's disease.

The patient experienced pain and constant edema in the ankles during the next 3 months. She developed numbness in the left side of the face and about her mouth, aggravated by cold. The mouth itself felt puckered, and the tongue tingled, without any relief after taking nicotinic acid. For 3 weeks before the second admission to the hospital, the swelling of the ankles had increased considerably, and the patient developed dyspnea and orthopnea, with a loose croupy cough.

The patient was admitted for the second time on November 22, 1939, when she appeared very ill, dyspneic and orthopneic, with pale and slightly cyanotic lips. The scleroderma and pigmentation were unchanged. The fundi were normal. There were signs of fluid in the chest on both sides posteriorly below the 7th interspace, extending well forward into the axillas. The apex impulse of the heart was palpable at the left anterior axillary line in the 5th interspace, and there was slight enlargement to the right. By percussion, no increase in supracardiac dullness was apparent. The heart action was regular and rapid, and the rate was 110, with sounds of fair quality; there were no murmurs. The pulmonic second sound was louder than the aortic second, and the blood pressure was 148/102. The abdomen was not remarkable except for tenseness suggestive of ascites. Neither the liver nor the spleen could be felt. There was marked edema of the lower extremities to the mid-thigh, and moderate pitting edema of the sacrum.

Laboratory studies showed a urine concentration varying from 1.010 to 1.020, with a very slight trace to trace of albumin, the sediment containing a few white cells, rare red cells, 2 to 4 granular casts and 1 or 2 hyaline casts per high-power field. The red-cell count was 3,720,000, with a hemoglobin of 10.2 gm. (70 per cent Sahli), and the white-cell count was approximately 18,000, with 87 per cent polymorphonuclears. A stool examination was negative for occult blood. The blood nonprotein nitrogen

was 42 mg. per 100 cc. on admission, and 62 mg. 2 days later. The blood cholesterol was 255 mg. per 100 cc., the sugar 120 mg., the carbon dioxide combining power 55 vol. per cent, the total protein 6.0 gm., the albumin 3.3 gm., and the globulin 2.7 gm. per 100 cc. The blood-chloride level was 440 mg. per 100 cc. X-ray study revealed enlargement of the heart, chiefly to the left, with diffuse haziness of the lung fields and mottling at the bases interpreted as showing congestive changes. The electrocardiogram revealed normal rhythm, a rate of 110, left-axis deviation, notched and widened QRS complexes, probable intraventricular block, deep S<sub>2</sub>, diphasic T<sub>1</sub>, elevated ST<sub>3</sub> and ST<sub>4</sub>, and a PR interval of 0.2 second.

On admission, the temperature was 100°F. by mouth, and rose to 101° before exitus. The pulse averaged 110 to 120, and the respirations 20. The patient was seen by a consultant, who wrote, "I believe that this woman is suffering from a diffuse arterial pathologic process that falls into the lupus erythematosus group." Treatment included high-vitamin diet, restriction of fluids, digitalis, and thiamin chloride intramuscularly and intravenously. On the night of the 2nd hospital day, the patient experienced an attack of pulmonary edema, which responded to morphine, atropine, tourniquets, venesection and oxygen by Boothby mask. On the following day, 750 cc. of thin amber fluid was removed from the right pleural cavity. The circulation time by the calcium gluconate method was 19 and 22 seconds. No diuresis resulted from the intravenous injection of 1 cc. of Mercupurin, nor from the similar administration of hypertonic glucose solution. The patient became semicomatose, developed marked difficulty in getting air in and out of the lungs, had convulsive twitchings, and died on the 5th hospital day.

*Autopsy:* The body showed good development and fair nourishment. Marked pitting edema was present in both lower extremities, extending almost to the crests of the iliums. In the exposed portions of the body, the skin was taut, inelastic and a shiny tan brown. This brownish pigmentation was most marked on the face and neck and over a collarlike area on the upper thorax. On the under surface of the tongue the mucous membrane had an irregular brownish pigmentation, and both buccal mucosae had small minute spots of brownish pigment. No lymphadenopathy was found. The fingers bilaterally revealed a peculiar firm nodularity of the terminal phalanges, not quite typical of clubbing. The skin in these areas was taut, tense and hard. No evidence of muscular atrophy was noted in either the upper or the lower extremities. On section, the musculature was of firm consistence and dark red brown.

There was 200 cc. of clear, straw-colored fluid in the peritoneal cavity, a total of 700 cc. in both pleural cavities, and 300 cc. in the pericardial sac.

The heart weighed 285 gm. and was increased in size, with moderate dilatation of the right side and definite hypertrophy of the left ventricle. The myocardium everywhere was of firm consistence. The valves and mural endocardium were normal. After injection and dissection, the coronary vascular tree appeared to be patent throughout both sides of the heart. The left ventricle measured 1.6 cm. in thickness, the right ventricle 0.5 cm.

The lungs, except for a small portion of each upper lobe, were solid and firm in consistence, with no palpable crepitation.

The spleen, which was of rather firm consistence, weighed 145 gm.

The liver weighed 1540 gm. and appeared normal except for slight congestion about the central areas.

Each kidney weighed 145 gm. The fibrous capsules

were thin, and stripped easily. The outer surfaces were smooth red gray, a slight fine granularity being visible and palpable. The cut surfaces were markedly congested, and the blood vessels stood out quite prominently in the cortex and the medulla, which were sharply demarcated. The cortex measured approximately 0.8 cm. in width, it was of uniform appearance, and the glomeruli were seen as minute pin points. No degeneration in the tubular regions was noted.

Both adrenal glands were of normal size and shape, with normal appearance on section. The remainder of the organs, including the thyroid and parathyroid glands and the brain, were not remarkable.

Cultures of the heart's blood and the pericardial fluid were sterile.

At microscopic examination, sections of the heart revealed extensive diffuse fibrosis throughout, especially marked on the right side. In some parts of the right ventricle most of the heart wall consisted of a condensed stroma and old avascular fibrous tissue, with scattered, small, slightly sclerotic blood vessels traversing the sheet of dense fibrous tissue. No acute arterial lesions were present in any of the sections, and there were no changes

subacute necrotizing arteriolitis (Fig. 1). The glomeruli were not decreased in number, but were swollen and increased in size, the swelling being especially marked in the basement membranes about the capillary loops in the tufts, which were widened and had a hyaline appearance. The afferent arterioles likewise were more prominent, owing to swelling of their basement membranes, but there was no chronic hyalinizing arteriolar sclerosis. The acute necrotizing inflammatory process chiefly involved a medium sized artery about the size of an interlobular artery. This reaction could be seen to spread into the afferent arterioles and then up into the capillaries of the glomeruli. The intimal coat was swollen and revealed



FIGURE 1. *Acute Necrotizing Arteriolitis and a Glomerulus with a Thickened Basement Membrane.*

suggestive of old healed arterial lesions, although the walls of the small arteries and arterioles revealed slight edematous thickening of their muscular coats. The valves were normal.

In the lungs, there was a diffuse pneumonic process, showing all stages of consolidation. Throughout the pulmonary tissues, the smaller blood vessels showed slight thickening, with edema of the medial muscular coats. In some places, one could note a ring of vacuoles, which appeared to separate the intimal coat from the media. Various sections revealed some fibrosis throughout the pulmonary tissue.

The arterioles around the adrenal capsule showed a slight but definite sclerosis of their walls. The parenchyma and cortex, however, were normal.

All sections of the kidneys revealed a diffuse acute and

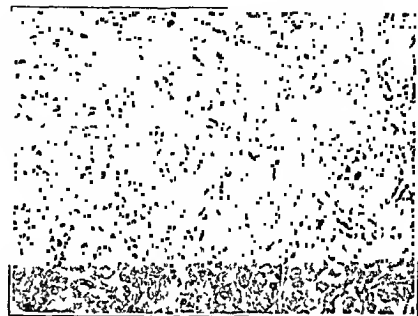


FIGURE 2. *Three Stages of Arteriolitis.*

*The arteriole on the extreme left is similar to that in Figure 1. Note the thickened wall and the cellular proliferation in the arteriole of the extreme right.*

marked proliferation of its cells, with marked narrowing of the lumen of the vessel. In many areas the walls of the arteries were edematous and necrotic, and were the site of deposits of purple-staining crescents of fibrin, with scatterings of polymorphonuclear cells. Several sites of rupture of the necrotic muscular medial coat of the artery, with exudation of polymorphonuclear cells into the surrounding stroma, were found. In other areas, this acute process appeared to be in the stage of healing, with lymphocytes predominating in the inflammatory infiltration and fibroblasts obliterating the vessel lumen. There was evidence of a completely healed stage, with small canalizing lumens that traversed the occluding mass of fibrous tissue within the former lumens of the vessels (Fig. 2). The tubules, as a whole, were slightly dilated, and their epithelial cells swollen and granular. There was only one wedge-shaped area of acute necrosis.

The parathyroid and thyroid glands were normal in all sections.

Sections of skeletal and diaphragmatic muscle presented no abnormalities of cells, stroma or blood vessels.

The epidermis revealed no atrophy, but the basal cells contained an increased amount of pigment. The dermis itself was slightly thickened. Scattered, otherwise normal, capillaries had a collar of lymphocytes about them. No degenerative changes in the collagen or elastic fibres could be seen.

The remainder of the sections, including those of the brain and cord, showed nothing worthy of remark.

The anatomic diagnoses were: acute and subacute necrotizing arteritis of kidneys, diffuse fibrosis of myocar-



dium; pigmentation of skin; chronic passive congestion of lungs and spleen; and confluent bronchopneumonia.

In many of its features, this case illustrates the classic characteristics of scleroderma. The history of Raynaud's disease, the sclerodactylia, the symptoms of arthritis with x-ray confirmation, and the temporary improvement with thyroid medication are typical. The sensitivity to sunlight, however, as manifested by deep and persistent bronzing of the exposed surfaces, was unusual, and reminiscent of the even more striking sensitivity noted in dermatomyositis and systemic lupus erythematosus. So intense was the pigmentation that the first hospital admission was for the express purpose of evaluating the possible presence of Addison's disease. A similar situation prevailed in the case reported by Talbott and his colleagues.<sup>1</sup> It is significant that throughout the first hospital stay the patient's temperature reached 99.4°F. daily and the pulse 90 while the patient was resting in bed, even after the minor local infection in the foot had completely subsided. This was definite evidence of a systemic reaction not usually seen in scleroderma. Evidence of renal involvement at this time was lacking; the urine analysis was negative, the nonprotein nitrogen of the blood was within normal limits, and the blood pressure was not elevated. Excretion of creatine, as often noted in scleroderma and dermatomyositis, was increased. At the time of the second hospital admission, three months later, failure of both the right and left sides of the heart was evident, and there were the albuminuria, microscopic hematuria and casts, and terminal azotemia seen in systemic lupus erythematosus and polyarteritis nodosa.

At post-mortem examination the extensive myocardial fibrosis, with adequate coronary circulation, and the pulmonary fibrosis were arresting findings, and recalled the marked increase in the connective tissue of the viscera reported by Matsui<sup>2</sup> in his cases of scleroderma. The striated muscle was normal. Neither the adrenal nor the parathyroid glands showed pathologic lesions. The kidneys in gross seemed essentially normal except for congestion, but microscopically they revealed widespread acute and subacute arteriolitis such as one would expect to find in a fulminating case of systemic lupus erythematosus. In this patient, the two basic pathologic changes of scleroderma—proliferation of connective tissue and alterations in the arterioles—were manifested in various internal organs. A case of diffuse scleroderma with identical changes in the renal arterioles, but without the visceral fibrosis, was reported by Masugi and Yä.<sup>3</sup>

## SCLERODERMA

Credit has been given to Curzio, of Naples, for the first description of an authentic case of scleroderma in 1752.<sup>4</sup> The condition occurs most frequently in the fourth and fifth decades, although people of all ages may be affected. The female sex predominates at least in the ratio of 2:1. The onset may be slow,—with prodromal symptoms of malaise, joint pains, asthenia and loss of weight,—or rather sudden, following a systemic infectious disease such as influenza. Other cases appear insidiously after a long history of Raynaud's disease. A smaller number of cases have followed acute arsenism. Two forms are recognized. The circumscribed type may consist of small patches of thickened skin, often about the neck (morphea), linear streaks along the course of nerves or blood vessels and sclerodactylia involving the fingers, usually in association with Raynaud's phenomenon. The diffuse form may arise from the circumscribed, or may appear first as a widespread involvement. Progressing with variable speed through the three stages of edema, induration and atrophy, the affected areas become brawny and hidebound. Pigmentation is common, from an ivory or yellowish tint to a deep bronze, especially over the exposed portions of the body, where it is indistinguishable from Addisonian coloring. Cutaneous sensation and both deep and superficial reflexes are usually well preserved. In half the generalized cases, the pain, swelling and stiffness of the joints simulate a severe and extensive arthritis. Atrophy of voluntary muscles, with contractures about the joints, serves further to limit motion. Involvement of the muscles of the tongue, soft palate and larynx is not uncommon. In one third of the cases, vasomotor disturbances are prominent. Calcification in the skin, often in the form of nodules, has been repeatedly noted. The eye grounds are normal. Aside from the progressive weakness and loss of weight, there are usually no constitutional symptoms until late in the disease. There is no fever, or any characteristic change in the blood other than a mild anemia. The basal metabolic rate is normal, and the blood calcium and phosphorus levels are usually not significantly altered. X-ray films of the hands are usually interpreted as showing osteoporosis and arthritic changes. Urinary excretion of creatine is definitely increased.<sup>5</sup> The course may be measured in weeks or years, and remissions are not unusual.

The pathology, extensively studied by Matsui,<sup>2</sup> is not limited to the skin, but affects all the viscera of the body, although one or more of the organs show a predominance of findings. The two



characteristic processes are proliferation of the connective-tissue stroma and changes in the small arterioles. The thickening of the connective tissue leads to rupture and disappearance of elastic fibers. In the blood vessels, there may be hypertrophy of the smooth muscle of the media, with infiltration of connective-tissue fibers, a thickening of the intima, with narrowing of the lumen, or complete obliteration, with thrombus formation. The changes in the skin and subcutaneous tissues exemplify both these processes. The epidermis is only slightly altered, whereas the corium shows hypertrophy of collagenous tissue, with obliteration of the papillas and replacement of fatty tissue, compression and atrophy of the sweat glands and hair follicles, and an obliterative endarteritis, with thickening of the media and adventitia and perivascular lymphocytic infiltration. There is atrophy, with similar changes in the voluntary muscles, subjacent or farther removed, and some general osteoporosis more marked in the affected regions, especially the terminal phalanges. The bone marrow becomes aplastic. Fibrosis of the lungs may occur and may result in pulmonary hypertension and dilatation of the right side of the heart. The kidneys often show changes in the blood vessels, with or without sclerosis of the glomeruli, tubular degeneration and general fibrosis. One or more of the endocrine glands commonly manifest atrophic or sclerotic changes.

Studies on the etiology of scleroderma have followed four main channels: endocrine dysfunction, vascular changes, disorders of the nervous system, and miscellaneous toxic and infectious agents.

The finding at autopsy of alterations in one or another of the endocrine glands, especially the pituitary and the thyroid gland, and the clinical evidence of glandular imbalance, occurring concomitantly in cases of scleroderma, have tended to implicate the glands of internal secretion. Matsui,<sup>2</sup> noting a diminution in the chromogenic cells of the pituitary gland, stressed its role in the pathogenesis. Others,<sup>6</sup> because of the Addisonian pigmentation and myasthenia, have suspected the adrenal glands. Most observers,<sup>7-9</sup> however, have considered the changes in function and histology of the endocrines to be secondary manifestations of the disease. They point out that scleroderma occurs with both hyperthyroidism and hypothyroidism, and consider that the beneficial effects that sometimes follow the use of thyroid medication are due to its local effect on the circulation of the skin and its general effect on metabolic processes. On the other hand, Leriche and Jung<sup>10</sup> maintain that scleroderma is a cutane-

ous form of chronic hyperparathyroidism, and advance considerable laboratory and clinical evidence in support of their views. In young pigs and rats, the injection of parathyroid extract has reproduced the disease. The calcium content of the skin in scleroderma is greatly increased, whereas the bones show osteoporosis. Surgical removal of the parathyroid glands in patients with scleroderma has resulted, according to Leriche and his associates,<sup>11</sup> in considerable improvement in most cases, and microscopic examination of the resected tissue usually shows hyperplasia. Leriche summarizes his opinion in the statement that the parathyroid glands are the primary, the bones are the intermediate, and the skin is the final site of the disturbance. Nevertheless, the data from metabolic studies are somewhat at variance with this concept. In hyperparathyroidism, the blood phosphorus content is low, the calcium is usually elevated, and urinary excretion of calcium is increased. In scleroderma, the blood levels of phosphorus and calcium are usually normal, and a negative calcium balance is lacking. The calcinosis of tissues may be due to local causes rather than to general hyperparathyroidism, and the osteoporosis is often confined to the affected regions.

The evidence that vascular changes play an important role in the causation of scleroderma is plentiful and impressive. Locally, the common association with Raynaud's disease, and the histologic demonstration of endarteritis and perivascular round-cell infiltration are classic features recognized by all investigators.<sup>2-4, 7, 9, 10, 12, 13</sup> Stokes<sup>3</sup> has considered that the basic disturbance is an endarteritis, the huge increase in connective tissue being essentially a fibrosis such as follows reduction in blood supply. That this lesion of blood vessels is fundamental and widespread, and not confined merely to the skin and underlying tissues, is indicated by the autopsy reports published by numerous observers.<sup>2, 11-16</sup> Marinescu and his co-workers<sup>14</sup> reported 5 cases of scleroderma, one of which at autopsy showed extensive arteriolar changes in the skin, heart, kidneys, nervous system and other organs. Matsui<sup>2</sup> described a case, with marked arteriolar changes in the kidneys and, to a lesser degree, in various other organs. The case reported in this paper offers further evidence along these lines.

The high incidence<sup>12</sup> of Raynaud's phenomenon in scleroderma has drawn attention to the part that the sympathetic nervous system plays in the disease. Brown and his associates<sup>17</sup> have investigated the factors of vasospasm and local disturb-

ances in the capillary bed. They found a sharp diminution in the number of open capillaries per unit area of skin, with the blood flow easily disturbed or slowed to a stop by lowering the temperature several degrees. The capillary loops were large, distorted and irregular, with outlines frayed and indistinct. They believed that although changes in vasomotor tone were important in scleroderma, they were not the primary cause. Clinically, the effects of sympathectomy and of Mecholyl iontophoresis have in some cases been beneficial. Sympathectomy has resulted in improvement in some cases not previously benefited by removal of the parathyroid glands, and the reverse has also been true. Lewis and Landis,<sup>18</sup> however, on the basis of considerable experimental study, believe that the role of the sympathetic nervous system is much less significant than purely local functional and structural changes in the digital arterioles in the circumscribed form involving the fingers.

Data concerning the relation of infectious and toxic agents to the pathogenesis of scleroderma are almost entirely clinical. The onset after erysipelas, hepatic infections and rheumatic states has led to the theory that the disease is a sequel of many infectious diseases. The appearance of scleroderma after acute arsenism or plumbism and the reports of increased amounts of arsenic or lead in the skin in some of these cases have inclined some observers to raise the question of a toxic origin of the condition.

#### DERMATOMYOSITIS

First described in 1887, independently by Hepp,<sup>19</sup> by Wagner<sup>20</sup> and by Unverricht,<sup>21</sup> who gave it its name, dermatomyositis presents a clinical syndrome that may vary widely. Most commonly it affects people of middle age, with children next in frequency, but cases at all ages and in both sexes have been described. There is usually an insidious onset, with prodromal symptoms for several weeks consisting of weakness, general malaise, anorexia or vomiting. The diagnostic triad of edema, dermatitis and myasthenia then appears, each varying in degree from case to case. In one fourth of the patients there is erythema and edema of the eyelids and face. The skin rash may be widespread, and usually possesses a peculiar heliotrope coloring often noted in disseminated lupus erythematosus. The eruption has been variously described as erysipeloid, roseolar, morbilliform, urticarial, eczematous and petechial, and may first appear after exposure to sunlight. In swift succession, manifestations of muscle disturbances follow. There are symmetrical muscle weakness, tenderness, swelling, brawny edema and pain on

active and passive motion. The patient may be rendered helpless. The muscles, firm and tense or soft and boggy, may be involved at a distance from the skin lesions. The skeletal muscles, especially those of the limbs, are chiefly affected, but in severe cases involvement of the muscles of deglutition, speech and respiration may result in symptoms resembling bulbar palsy. Splenomegaly is not uncommon. The temperature is usually remittent from a level of 101°F., but may exceed 103° or fever may be entirely absent. Tachycardia out of proportion to the temperature is often noted. An elevation of the white-cell count is usual, with eosinophilia in approximately one fifth of the cases. The urine often contains albumin, with pronounced creatinuria. The mortality averages 50 per cent, and death may occur from pneumonia, pleurisy or pericarditis. If the patient survives this stage, the edema subsides and the degenerative and inflammatory reactions in the muscles and skin may proceed to atrophy, fibrosis and contractures, especially at the elbows and knees. Osteoporosis occurs late, and the skin may take on a boardlike thickening identical with that observed in scleroderma. In mild cases, remissions or complete recovery may take place.

The pathology in the early stages, as determined by biopsy, is indistinguishable from that of early scleroderma. The skin, subcutaneous tissue and muscles are involved. The picture is one of edema, swelling of the endothelial cells lining the vessels, and perivascular and diffuse infiltration by lymphocytes and plasma cells.<sup>16</sup> Keil<sup>22</sup> has stated that in many cases of dermatomyositis the fundamental pathologic alteration occurs in the vasculature, with secondary implication of the muscle parenchyma. Numerous observers have expressed similar views, but there is no general agreement on this point. The muscle fibers present various disintegrative changes, ranging from swelling and loss of cross striations to vacuolar or hyaline degeneration. The similarity to the findings in thyrotoxicosis and myasthenia gravis has been noted.<sup>23</sup> According to Brock,<sup>24</sup> biopsy at a later stage in scleroderma shows thick-walled vessels, with the lumens narrowed or occluded, and an increase of the connective tissue in the sheaths and interstitial spaces of the muscles, with subsequent myosclerosis, whereas in dermatomyositis the cellular infiltration and degeneration of the muscle parenchyma itself persist to the end and the vascular changes are minimal. This observer found a diffuse increase in connective tissue in the heart at one post-mortem examination.

Various features of the disorder have suggested an inflammatory or infectious etiology.<sup>25</sup> The frequent occurrence of first symptoms after a fe-

brile disturbance such as tonsillitis and influenza, the fever, albuminuria and splenomegaly in some cases and the relapsing character of many cases all appear to point in this direction. Bacteriologic studies, however, have been almost uniformly negative. Keil<sup>22</sup> has discussed the factor of lead as a vascular poison in the pathogenesis of this and similar diseases, citing cases from his own experience and from the literature, but the evidence is based on association and analogy and is not entirely convincing. The concept that dermatomyositis may be a primary disturbance of the blood vessels was first proposed by Lépine,<sup>26</sup> who suggested the term "angiomyositis." Köster,<sup>27</sup> in a report of a series of cases with microscopic data, emphasized repeatedly the importance of the blood vessels in the pathogenesis of the condition. Fahr<sup>28</sup> also believed that in many cases of dermatomyositis the initial fundamental disturbances are in the blood vessels supplying the affected muscles, the alterations being a form of necrotizing arteriolitis. Equally significant is the relation of dermatomyositis to scleroderma. The cardinal pathologic alterations in the blood vessels and connective tissue of skin, muscles and other organs are considered identical in both conditions, although varying in degree and distribution.<sup>27, 29</sup> Other observers, however, do not agree with this opinion. Clinically, the evidence of a close relation is so impressive that many consider the two conditions as one disease. The literature since 1900 is replete with records of carefully observed cases diagnosed and reported as scleroderma, later assuming the classic feature of dermatomyositis, and the reverse has occurred even oftener.<sup>23-25, 30</sup> Many transitional cases are also reported.<sup>16, 21, 22</sup> In both diseases, a history of antecedent Raynaud's disease is common, edema is an initial symptom, joint pains are present, the pharynx and larynx may be affected, creatinuria is present, renal involvement with albuminuria may be evident, and calcification or pigmentation may occur. The diagnostic difficulties have been commented on by Brock,<sup>24</sup> who found that even biopsies were misleading until late in the disease. Without a biopsy of muscle the differentiation of dermatomyositis from trichinosis may be impossible. In the latter, involvement of the eye muscles and diaphragm occurs much more commonly than in dermatomyositis.

#### DISSEMINATED LUPUS ERYTHEMATOSUS

In his memorable reports of an "erythema group" of diseases with visceral manifestations, Osler<sup>31</sup> contributed greatly to the evolution of the present concept of systemic disease associated with

cutaneous manifestations. Of such syndromes, acute and subacute disseminated lupus erythematosus (as distinguished from the fixed and generalized discoid types) is a notable example. First described by Kaposi<sup>34</sup> in 1872, this disease shows a marked predilection for females, usually in the second to fourth decade of life. Nevertheless, cases have been reported in both sexes, at all ages and in many races and countries. Constitutional symptoms may far overshadow the cutaneous eruption, and often precede it for weeks or months. There may be a prolonged and insidious onset, with fatigue, exhaustion, disability, low-grade fever and joint pains, often diagnosed as rheumatoid arthritis or rheumatic fever. With the appearance of skin lesions or signs of visceral disturbances, the true nature of the serious underlying condition becomes apparent.<sup>35</sup> In the fulminating case, the constitutional and skin manifestations appear abruptly and simultaneously, the temperature exceeds 103°F, prostration is extreme, the sensorium is clouded, and stupor or delirium occurs. The dermatitis usually begins on the face or upper part of the thorax and neck as areas of indefinite superficial erythema that coalesce and become well demarcated. Edema of the eyes and face is often marked. There is rapid extension to the extremities, with involvement of the finger tips. The eruption, favoring the exposed surfaces, is bright reddish violet, often with a cyanotic tinge in the active areas. Petechial, purpuric, papillar or bullous lesions are seen, but indurated plaques with epithelial plugging, scaling and atrophy are rare. When involution occurs, residual pigmentation of various types may follow, and may simulate the extensive deep pigmentation of Addison's disease. Undue exposure to sunlight has precipitated the first appearance of the rash and an intensification of the constitutional reaction in a considerable number of cases. Local or generalized adenopathy is described. The systemic symptoms are almost infinite in variety. Involvement of the serous surfaces, including synovia, pleura, pericardium and endocardium, is common. Pain in the form of arthralgia, myalgia and neuralgia appears early and may be severe. Gastrointestinal symptoms vary from nausea, vomiting and diarrhea to crises of abdominal pain at times so marked as to result in surgical exploration. In a small proportion of the cases, the spleen is enlarged. In some cases, ophthalmoscopic examination reveals perivascular hemorrhages and fluffy exudates. Evidence of renal damage, with albuminuria, microscopic hematuria and casts, is a feature of the condition, but the blood pressure is usually not significantly elevated. Terminal

azotemia is frequently noted, and nephrotic syndromes have been described. The urinary findings are not consistently characteristic of any one type of renal lesion. There is often depression of the bone marrow, with secondary anemia, leukopenia and thrombopenia, a rise in the white-cell count usually signaling a serious and terminal complication. Serologic tests for syphilis may be falsely positive. Cultures of the blood have given equivocal results. The course in the acute fulminating cases is progressively downward, whereas in the more chronic types recession of the eruption and of the constitutional symptoms occurs only to be followed by an exacerbation months later. The mortality exceeds 90 per cent in the acute cases, and averages 50 per cent in the milder forms. Death may result from pneumonia, pericarditis, meningitis or uremia. The prognosis is indicated more accurately by the severity of the general reaction than by the extent of the cutaneous processes, which are helpful in diagnosis.

The characteristic pathologic features are found in the minute blood vessels, and consist of widespread proliferative changes in the endothelium, with a tendency to thrombus formation, or of a degenerative or necrotizing process in the walls, often with hemorrhage into adjacent tissues. These changes, however, are not specific for a <sup>57</sup>one disease. In disseminated lupus erythematosus, the changes in the skin are of minor importance and without diagnostic significance.<sup>30</sup> Thinning of the epidermis, atrophy of the sebaceous glands and hair follicles, edema of the cutis and marked dilatation of the superficial blood vessels and lymph spaces, with extravasation of blood and serum, are the essential findings. Most striking are the lesions in various organs throughout the body, especially the kidneys, heart, lungs, liver and serous surfaces. Considerable variability is seen in the general distribution of these lesions and in the viscera principally affected, but the kidney is most frequently involved. In gross these organs usually show little of significance, and have been discarded frequently without investigation. Microscopic study reveals hyaline thickening of many glomerular afferent vessels, with secondary thrombi, fibrosis and recanalization. The glomeruli themselves may be implicated, with a homogeneous thickening of the capillary wall described as a "wire-loop" effect.<sup>37-41</sup> At times a focal or diffuse panarteritis is found, with involvement of all the coats of the vessels, necrosis of the media, proliferation of the intima, secondary thrombi and periarterial accumulations of cells.<sup>42-44</sup> Stickney and Keith<sup>15</sup> found the renal arterioles to be essentially

normal in most of their cases, whereas the glomerular capillaries showed proliferation of the endothelial cells, hyaline thickening of the capillary walls and changes in the basement membrane, similar to the alterations in the toxemias of pregnancy, ulcerative colitis and peritonitis. Renal lesions were also noted by Snapper,<sup>40</sup> O'Leary<sup>47</sup> and Montgomery,<sup>48</sup> who commented on their similarity to the findings in eclampsia. In a considerable proportion of the cases, there is an endocarditis of varying type, with and without associated Aschoff bodies in the myocardium. Pericarditis, pleurisy, synovial changes, splenic infarcts, hepatic and gastrointestinal lesions, and terminal pneumonia constitute the remaining predominant changes seen post mortem.<sup>49</sup> On the other hand, Montgomery<sup>50</sup> was unable to discover any characteristic obliterative changes in the smaller blood vessels either in the internal organs or in the skin, and Mallory<sup>51</sup> has found no lesion that he considers pathognomonic of disseminated lupus erythematosus.

The etiology of the disease remains unknown. Innumerable theories have been advanced to explain its pathogenesis. Most observers favor the view that it is an infection, perhaps streptococcal, and others stress the relative frequency of a tuberculous background. Goeckerman<sup>52</sup> has considered it as a response to a septic infection conditioned by a previously established tuberculous allergy. O'Leary,<sup>53</sup> however, believes that the disorder is due to a toxemia, probably attributable to a bacterial agent. The frequent recovery of the tubercle bacillus in blood cultures, as reported by some investigators, has not been confirmed. Tuberculous adenitis is surprisingly prevalent. Streptococci of various types are often isolated in the terminal stages, but their primary role is open to doubt. The condition has been attributed to trauma in the form of drugs and heat, sensitivity to light, toxic factors, various metabolites, focal infection, disease of the bone marrow and disease of the reticuloendothelial system. Ludy and Corson<sup>54</sup> believe that the action of ultraviolet light in constitutionally susceptible people is a factor, and that a heavy metal like lead may serve as a catalyst. In almost half their cases, they found hematoporphyrinuria, but the attempts of numerous other investigators to detect this substance in the urine have been unsuccessful. The common observation that signs of a prolonged and severe systemic disturbance have antedated the appearance of the skin lesions indicates that sunlight can have only the secondary effect of determining the onset and localization of the dermatitis. The problem is whether disseminated lupus ery-

thematosis is a pathologic entity due to a specific if unknown cause, or whether it is a peculiar reaction of the internal organs and skin initiated by a variety of different agents. Madden<sup>55</sup> regards the various clinical forms as manifestations of one disease, differing only in the severity and distribution of the lesion. Denzer and Blumenthal,<sup>41</sup> recognizing that the vascular changes are the only conspicuous pathologic finding, nevertheless refuse to regard them as the sole basis of the disease and postulate an underlying more fundamental pathologic disturbance.

Although the disease is commonly considered as a problem for the dermatologist, the internist may see these patients first if the systemic complaints precede the onset of the dermatitis, if the skin eruption is mild and inconspicuous, or if the clinical course is fulminating, with severe constitutional symptoms. Diagnosis, as Mook and his associates<sup>58</sup> point out, is elusive and difficult. When the cutaneous manifestations predominate, a variety of skin diseases are simulated. If the systemic reaction is marked, typhoid fever, pyemia, malignant endocarditis and rheumatic fever must be considered. During crises of abdominal symptoms, surgical intervention for possible appendicitis, cholecystitis or perforated duodenal ulcer has seemed imperative.

The relation of systemic lupus erythematosus to dermatomyositis, and less directly to scleroderma, is suggested and supported by both clinical and pathological evidence. Raynaud's phenomena may precede or accompany the disease in all three. Subcutaneous calcification and pigmentation on the exposed surfaces, reaching Addisonian intensity, may occur in all three. There is hypersensitivity to sunlight with aggravation of the condition in both systemic lupus erythematosus and dermatomyositis. There are numerous reports<sup>19, 56</sup> in the literature, of which only a few are cited, describing cases diagnosed as disseminated lupus erythematosus by one or more competent dermatologists and later showing the typical features of dermatomyositis. Turner<sup>57</sup> reported a definite case of dermatomyositis that in a recurrence exhibited the skin lesions and constitutional symptoms of lupus erythematosus disseminatus. Montgomery<sup>58</sup> has also pointed out the clinical similarities of these two conditions. Dowling<sup>59, 61</sup> considers that the vascular changes of scleroderma and dermatomyositis are of the same order, and much like those of disseminated lupus. Visceral lesions, with involvement of the smaller blood vessels, occur in all three conditions.

## • THE LIBMAN-SACKS SYNDROME

First described in 1924, the features of the Libman-Sacks<sup>58</sup> syndrome were listed as prolonged fever, an atypical verrucous endocarditis, absence of Aschoff bodies in the myocardium, white-centered petechiae in the skin, signs of renal disease and consistently negative blood cultures. In several patients, skin lesions indistinguishable from those of disseminated lupus erythematosus were noted. In 1931, Baehr,<sup>59</sup> discussing the renal lesions seen in 17 cases, reported that unusual vascular changes were found not only in the kidneys but in other internal organs, and that most but not all cases had skin manifestations characteristic of disseminated lupus. The syndrome then included pleural effusion, pericarditis, arthritis and leukopenia. By some observers it was considered as a separate entity; others regarded it as one of Osler's erythema group, and a few included it in the many variables of subacute disseminated lupus erythematosus. In a subsequent paper Baehr<sup>49</sup> detailed the clinical and pathological data in 23 cases of disseminated lupus, in 13 of which the coarse verrucous endocarditis of the Libman-Sacks syndrome without Aschoff bodies was found. Twenty of these cases presented disseminated vascular lesions in the kidneys and other viscera. It was then apparent that endothelial damage, which might involve the valvular endocardium or not, was the outstanding feature of this group of cases, and the unusual endocarditis that originally drew attention to the syndrome assumed a position of secondary importance. In his pathological studies of systemic lupus, Montgomery<sup>48</sup> found endocarditis in 7 of 15 cases, in each one associated with Aschoff bodies in the myocardium. Belote and Ratner,<sup>60</sup> Denzer and Blumenthal,<sup>41</sup> Keil<sup>61</sup> and Montgomery<sup>56</sup> have identified the Libman-Sacks syndrome more or less definitely with disseminated lupus erythematosus. It is of interest that it has never been reported in scleroderma or dermatomyositis.

## POLYARTERITIS NODOSA

Under the name "periarteritis nodosa" a voluminous literature has accumulated concerning a disease characterized by widespread segmental lesions in the smaller arteries and arterioles. Occurring at all ages, but most commonly between ten and forty, the condition affects males four times as frequently as females. The onset may be abrupt or gradual, with fever, muscular pains, general weakness, abdominal pain and edema. The temperature reaches 101°F., may be constant

or intermittent, and is associated with a tachycardia out of proportion to the temperature level. Polymyositis in the extremities and polyneuritis of peripheral type are common. Cramplike or colicky abdominal pain occurs in most cases. Nodules, firm and nontender, may appear in the later stages along the course of superficially placed arteries and thus establish the diagnosis on clinical grounds or by biopsy. Cutaneous lesions of many types are described. Leukocytosis, secondary anemia and albuminuria, with microscopic hematuria and casts, are almost constant features. Hypertension is a relatively late manifestation and is usually of renal origin. Later, there is cardiac failure without obvious cause, and bronchiolitis with prominent cough. The presenting symptomatology has been grouped as renal, abdominal, neuromuscular, cardiac and bronchial. The duration of the disease is usually measured in months, and the prognosis is extremely unfavorable.

With the recognition that the media rather than the adventitia was the primary seat of the lesion and that all the coats of the vessels were involved, Haining and Kimball<sup>62</sup> proposed the name "polyarteritis nodosa." In addition to inflammatory changes in the adventitia, Leishman<sup>63</sup> described necrosis of the media, rupture of the internal elastica lumina, proliferation of the intima and thrombosis, at times with recanalization. In the early stages, the characteristic local cellular reaction is a polymorphonuclear one, with a large percentage of eosinophils.<sup>64</sup> In order of frequency, the organs involved are the kidneys, heart, liver, spleen, lungs, mesentery, skeletal muscles and nervous system. O'Hare and his associates<sup>65</sup> have noted the resemblance of the pathology to that of the rickettsial diseases. Fahr<sup>28</sup> considered that the arteriolitis of dermatomyositis might be allied to that of periarteritis nodosa.

Suggestions concerning etiology include streptococci, syphilis, parasites, viruses and allergic factors. Two opposing schools of thought are exemplified by Moschowitz,<sup>66</sup> who maintains that periarteritis nodosa is not a primary clinical or morphologic entity but a complication of various widely divergent conditions, and by Haining and Kimball,<sup>62</sup> who, believing that it is due to a specific infection, possibly with a virus, point out that if it is a manifestation secondary to infection it should occur much oftener.

#### DISCUSSION

It is evident from the descriptions of these diseases that a differentiation on a clinical basis should be possible in most cases.

In scleroderma, there is a preponderant incidence in the fourth and fifth decades and in women; antecedent vasomotor disturbances in one third of the patients; the triad of edema, induration and atrophy of the skin; arthritic manifestations, localized osteoporosis and secondary atrophy of voluntary muscles; absence of fever or other constitutional symptoms until late; and a chronic course, with relatively favorable prognosis. Although changes in the small arterioles and proliferation of the connective-tissue stroma may be found throughout all the viscera and in many of the muscles, resulting systemic disturbances that can be detected clinically are relatively uncommon.

Dermatomyositis occurs more commonly in children as well as later in life, is preceded by prodromal symptoms, and presents a diagnostic triad of edema, dermatitis, with sensitivity to sunlight, and myasthenia. Muscular pain, tenderness and swelling are common. A constitutional reaction is evidenced by fever, tachycardia, albuminuria, leukocytosis, occasional eosinophilia and splenomegaly. The prognosis is guarded, with an average mortality of 50 per cent. The pathologic changes involve the small blood vessels and the musculature, the skin being secondarily affected in the typical cases.

Disseminated lupus erythematosus is seen classically, although not invariably, in females of the second to fourth decade, and is characterized by constitutional symptoms of smoldering or fulminating intensity that precede, follow or appear abruptly with the cutaneous eruption. As in dermatomyositis, exposure to sunlight may aggravate or initiate both the rash and the general symptoms. The prostration, fever, tachycardia, arthralgia, gastrointestinal symptoms and involvement of serous surfaces, together with evidence of renal disturbance and depression of the bone marrow, all indicate the severity of the systemic reaction. The ultimate prognosis is poor. The pathologic changes, which remain the subject of much controversial discussion, are not peculiar to this disease. There are widespread proliferative changes in the endothelium of the minute blood vessels, at times with degenerative or necrotizing processes in the walls, varying considerably both in intensity and in distribution in individual cases. In some patients, involvement of the endocardium with an atypical verrucous process has led to the description of the Libman-Sacks syndrome.

Polyarteritis nodosa is seen most commonly between the ages of ten and forty, and in males much more frequently than in females. The general systemic disturbance is characterized by fe-

ver, myalgia, leukocytosis, abdominal pain and renal involvement, with albuminuria, microscopic hematuria and casts. Cutaneous lesions may occur, but are easily distinguished from the eruption of dermatomyositis and disseminated lupus erythematosus. In some cases the appearance of nodules along the course of superficial arteries settles the diagnosis. The pathologic lesions consist of a segmental involvement of the small arteries and arterioles that starts usually in the media, involves all the coats of the vessels and leads to a characteristic local polymorphonuclear cellular reaction, with a large percentage of eosinophils. The kidneys are most markedly affected. The disease runs a downward course over a period of months.

Efforts to group the various conditions discussed in this report under the heading of diffuse vascular disease or mesenchymal disease have been criticized as an attempt at oversimplification that does not actually contribute to an understanding of the fundamental pathogenesis of these disorders. Differences do exist in the extent of the pathologic changes, the size of the vessels involved, the organs chiefly affected and the resultant clinical picture. Nevertheless, if it is recognized that the classification is a broad and tentative one, there can be no serious objection.

Three important and perplexing questions arise in a survey of these diseases. What is the essential significance of the changes in the blood vessels? What agents or mechanisms bring about these alterations? Are various members of this group different clinical manifestations of the same disease? One enters immediately on highly controversial ground.

Although the vascular pathology must be considered the most constant histologic finding, in many cases the changes are so slight and the distribution so limited that they scarcely explain the varied clinical pictures and the frequent fatal results. Occasionally no blood vessel alterations whatever can be demonstrated, so that Mallory<sup>51</sup> and others have come to believe that there is no pathognomonic pathology in systemic lupus erythematosus and similar conditions. A conservative attitude, such as that of Denzer and Blumenthal,<sup>52</sup> seems best—namely, that the vascular lesions are merely a manifestation of an underlying pathologic process that in its progress frequently leads to morphologic changes in the small blood vessels.

Equally obscure are the etiologic agents causing these changes, and the mechanism by which the effects are produced. The very multiplicity of suggested factors indicates the confusion that surrounds this problem. The role of constitutional

susceptibility is repeatedly stressed in the literature. An example of this concept is seen in systemic lupus erythematosus, which is attributed by some to a response to a streptococcal infection in a patient previously sensitized by tuberculous allergy. The possibility of some form of toxemia is given impetus by the similarity of the renal lesions to those found in some cases of eclampsia. Various observers maintain that these diseases are distinct entities produced by specific if unknown causes, and point out the resemblance of the vascular lesions to those seen in rickettsial diseases, such as typhus. On the other hand, it is generally agreed that polyarteritis nodosa can be a sequel to a number of infectious and toxic conditions.

Most disconcerting have been the cases, diagnosed by careful clinicians as typical of one disease, that have progressed and assumed the classic clinical and histologic features of another in the group. Many of these transitional cases are reported. The logical consequence of this transition has been the tendency to identify dermatomyositis with scleroderma, and disseminated lupus erythematosus with dermatomyositis. Since the diagnosis must almost always be a clinical one without the confirmation that laboratory tests might give, it is probable that most of these cases represent diagnostic errors demonstrated with the passing of time. All the diffuse vascular diseases possess many symptoms and signs in common, and the placing of undue emphasis on any one of these may lead to unwarranted interpretations and conclusions. It is clear that in the final stages, dermatomyositis may be associated with the atrophic cutaneous changes of scleroderma, and that advanced scleroderma may include the extensive muscle atrophy and degeneration seen in dermatomyositis. Most of the confusion between the latter condition and systemic lupus erythematosus has arisen from the character and distribution of the rash and the associated myasthenia. Until further information is available, it seems best to consider these several diseases as clinical entities and to regard a diagnosis in the early phases as only tentative.

#### SUMMARY

Clinically, there are characteristic syndromes that correspond to the diagnostic terms of scleroderma, dermatomyositis, disseminated lupus erythematosus and polyarteritis nodosa. Not infrequently, however, patients present symptoms and signs that form essential characteristics of two or more of these conditions.

Since the diagnosis is almost always a clinical one without laboratory confirmation, the placing of undue emphasis on certain features may lead

to diagnostic errors and a tendency to identify one disease with another.

There is no unanimity of opinion regarding the specific and fundamental pathology of certain of these syndromes, all of which represent a widespread vascular involvement, differing usually in the extent of the pathologic change, the size of the vessels involved, and the organs chiefly affected.

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## TUBERCULOSIS OF THE STERNUM\*

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**T**UBERCULOSIS rarely involves the sternum. In 1134 cases of bone and joint tuberculosis admitted to the Lakeville State Sanatorium from 1926 to 1940, the diagnosis of tuberculosis of the sternum was made in only 12, an incidence of 11 per cent. References in the literature consist essentially in a few isolated case reports<sup>1,2</sup>

symptom in 7 cases, whereas pain was an early symptom in only 3. In 2 cases a discharging sinus was the chief complaint.

Eventually, practically every case develops one or more draining sinuses, and in about a third of the cases the sinuses are multiple. Figure 1 depicts the general distribution of these sinuses. It can readily be seen that any portion of the sternum or its adjacent structures may be involved, hence, the exact location of these sinuses is of no diagnostic significance.

Careful study of the material discharging from

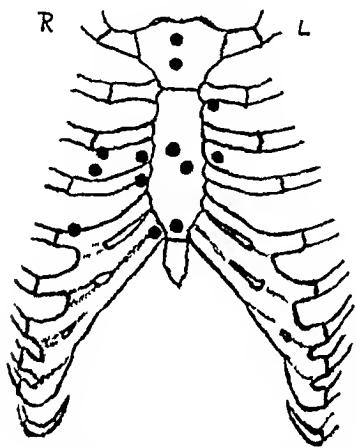


FIGURE 1 *Approximate Distribution of Sinuses in Patients with Tuberculosis of the Sternum*

This paper presents a study of these 12 cases, 9 of which were followed for an average of more than five years.

The 12 cases were about equally divided as to sex: 7 females and 5 males. The ages of the patients at the onset of symptoms varied from one and a half to seventy years, and there was no preponderance of any age group. In no case was there a history of trauma. There was a definite history of contact with tuberculosis, however, in 5 cases.

Tuberculosis of the sternum must be suspected when a patient who has a tuberculous focus elsewhere in the body develops a swelling on the anterior chest wall. Eleven of the 12 patients had other tuberculous lesions. A painless swelling in the region of the sternum was the presenting

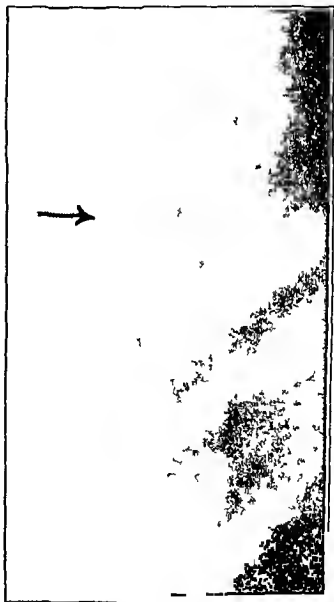


FIGURE 2 *Lateral View of Sternum in a Two-Year Old Child (Case 12)*

*Note the area of rarefaction in the manubrium. The lesion healed clinically and roentgenologically without operation.*

the sinuses, however, is essential. Indeed, it is often difficult to make a correct diagnosis before a sinus develops. Material that drains or is obtained at operation should be subjected to thorough pathological study, including guinea pig in

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oculation. In 8 of the cases, such material confirmed the diagnosis of tuberculosis: 2 by guinea-pig test alone, 2 by biopsy alone and 4 by both methods. In 4 cases, the diagnosis was made only on clinical and roentgenographic evidence.

Tuberculosis of the sternum must be differentiated from tuberculosis of the chest wall and tu-

coma of the sternum may simulate tuberculosis roentgenographically, according to Cella Maggani,<sup>4</sup> but since the sternum is readily accessible surgically, a biopsy specimen should be taken whenever there is the slightest doubt. Other tumors, such as cysts, lipomas and fibromas, may also be ruled out by biopsy.

TABLE 1. *Analysis of Cases.*

CASE No.	SEX	AGE AT ONSET OF SYMPTOMS	PRESENTING COMPLAINT	OPERATION	PATHOLOGICAL CONFIRMATION OF DIAGNOSIS	ASSOCIATED TUBERCULOUS LESIONS	COMMENT
1	F	17	Discharge	Incision and drainage	No	Trochanter Kidney	Followed 2 10/12 years, no recurrence of disease of sternum.
2	M	10	Swelling	Incision and drainage, curettage, and biopsy	Yes	Lymph nodes Spine	Discharged in poor condition at parent's request, followed 2 7/12 years, then lost (probably dead).
3	F	10	Discharge	None	No	Lymph nodes Spine Lungs	Had one sinus which stopped draining one week after admission, followed 11 3/12 years, no recurrence of sternum disease, works as nurse.
4	M	19	Swelling	Aspiration	No	Ankle Lungs Bowel	Left at own request against advice; had two sinuses died 3 8/12 years later of pulmonary tuberculosis
5	F	67	Swelling	None	Yes	Ankle	Sinus healed 2 years after discharge, patient later developed Pott's disease; followed 4 3/12 years, died of arteriosclerosis in an insane asylum.
6	M	22	Swelling	Aspiration	Yes	Finger Lungs	Had four sinuses in all, has not worked since discharge, followed 3 7/12 years, has far advanced pulmonary tuberculosis at present.
7	F	70	Swelling	Incision and drainage	Yes	Lymph nodes Ribs Pleura Lungs	Died 7 months after admission, autopsy revealed extensive tuberculosis of chest and arteriosclerosis
8	F	40	Swelling	Excision of costal cartilage	Yes	Lymph nodes	Sinus healed 7 months after admission, followed 10 5/12 years, has had no recurrence of sternum disease.
9	F	26	Pain	Aspiration and resection of sinuses	Yes	Chest wall Peritoneum	Followed 10/12 years, slight drainage period from three pin point sinuses
10	M	56	Pain	Incision and drainage, and biopsy	Yes	None	Left at own request against advice, followed for 7 4/12 years, no recurrence of disease at sternum, bedridden past 3 years
11	M	46	Pain	Curettage	Yes	Spine	Still hospitalized, has open granulating wound over manubrium, with purulent drainage.
12	F	1½	Swelling	None	No	Finger Spine Lungs	Still hospitalized, sinuses are healed

berculosis of the ribs and costal cartilages.<sup>3</sup> Tuberculosis may also involve the lymphatic vessels situated in the anterior costal interspaces, as well as the internal mammary or sternal lymph nodes, and necrotic nodes in this area may give rise to abscesses. In female patients, tuberculosis of the breast must occasionally be considered. The injection of a radio-opaque substance under such circumstances readily gives the clue to the actual process. A negative tuberculin test helps to distinguish chronic nontuberculous osteomyelitis of the sternum from tuberculosis and is therefore of value. Syphilis can be identified by the Wassermann test and by the fact that syphilitic lesions usually heal rapidly with specific treatment. Sar-

In 25 per cent of the cases, the tuberculosis of the sternum became arrested spontaneously and the sinuses healed. In the remaining 75 per cent, a variety of operative procedures were performed, such as aspiration, incision and drainage, curettage and the resection of sinuses. Since these operations were performed by different surgeons in different hospitals, accurate evaluation is difficult. Aspiration was performed in 3 cases, in two of which further operation was unnecessary; in the third, resection of sinuses was performed later. Herrick<sup>1</sup> also reported a patient in whom aspiration was performed and whose lesion healed under conservative treatment. In the other cases, incision and drainage were done at least four times.

nd curettage at least twice. The operative end results were usually good, regardless of the procedure followed.

With the aid of social service, a follow up was possible in all the cases discharged from the sanatorium. Two patients in this series (Cases 11 and 12) are still hospitalized, and a third (Case 13) died while in the sanatorium. Autopsy in this last case revealed tuberculosis of the sternum, ribs, pleura, pericardium, mediastinum and anterior chest wall. Of the 9 discharged patients, 2 (Cases 4 and 5) have died, one of pulmonary tuberculosis, and the other of arteriosclerosis. In neither was there recurrence of the disease in the sternum. A third patient (Case 2), a Chinese boy in ex-

no swelling, pain or tenderness. One of the patients (Case 6), however, has far advanced pul-

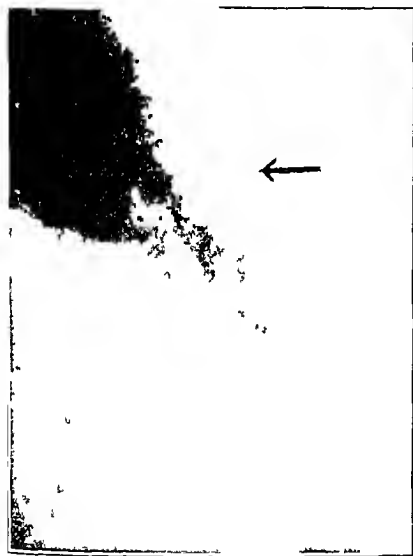


FIGURE 3 Lateral View of Manubrium (Case 11)  
The outline is irregular and there are many small rarefied areas within the bone

tremely poor condition, was taken by one of his parents to China and probably died en route.

Six cases were followed from ten months to eleven years and three months, with an average of over six years. In only one patient (Case 9), followed only ten months, does slight drainage persist. None of the other patients have had any recurrence of the disease in the sternum. All sinuses have remained healed, and there has been



FIGURE 4 Lateral View of Xiphoid Process (Case 10)  
Note the irregular contour and the areas of apparent bone destruction

monary tuberculosis, and another (Case 10), has been bedridden for three years because of a cerebral hemorrhage. In no fatal case in this series could tuberculosis of the sternum be regarded as a cause of death.

#### SUMMARY AND CONCLUSIONS

Twelve cases of tuberculosis of the sternum are reviewed. Sternal tuberculosis is almost invariably secondary to other demonstrable tuberculous foci. Painless swelling in the region of the sternum is the usual presenting symptom. The end results of conservative treatment are consistently good, radical surgery is apparently unnecessary.

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oculation. In 8 of the cases, such material confirmed the diagnosis of tuberculosis: 2 by guinea-pig test alone, 2 by biopsy alone and 4 by both methods. In 4 cases, the diagnosis was made only on clinical and roentgenographic evidence.

Tuberculosis of the sternum must be differentiated from tuberculosis of the chest wall and tu-

coma of the sternum may simulate tuberculosis roentgenographically, according to Cella Mariani,<sup>4</sup> but since the sternum is readily accessible surgically, a biopsy specimen should be taken whenever there is the slightest doubt. Other tumors, such as cysts, lipomas and fibromas, may also be ruled out by biopsy.

TABLE 1. *Analysis of Cases.*

CASE NO.	SEX	AGE AT ONSET OF SYMPTOMS	PRESENTING COMPLAINT	OPERATION	PATHOLOGICAL CONFIRMATION OF DIAGNOSIS	ASSOCIATED TUBERCULOUS LESIONS	COMMENT
		Jr.					
1	F	17	Discharge	Incision and drainage	No	Trochanter Kidney	Followed 2 10/12 years; no recurrence of abscess of sternum.
2	M	10	Swelling	Incision and drainage, curettage, and biopsy	Yes	Lymph nodes Spine	Discharged in poor condition at parent's request; followed 2 7/12 years; then lost (probably dead).
3	F	10	Discharge	None	No	Lymph nodes Spine Lungs	Had one sinus which stopped draining one month after admission; followed 11 3/12 years; no recurrence of sternum disease; works as nurse.
4	M	19	Swelling	Aspiration	No	Ankle Lungs Bowel	Left at own request against advice; had two sinuses; died 3 8/12 years later of pulmonary tuberculosis.
5	F	67	Swelling	None	Yes	Ankle	Sinus healed 2 years after discharge; patient later developed Pott's disease; followed 4 3/12 years; died of arteriosclerosis in an insane asylum.
6	M	22	Swelling	Aspiration	Yes	Finger Lungs	Had four sinuses in all; has not worked since discharge; followed 3 7/12 years; has advanced pulmonary tuberculosis at present.
7	F	70	Swelling	Incision and drainage	Yes	Lymph nodes Ribs Pleura Lungs	Died 7 months after admission; autopsy revealed extensive tuberculosis of chest and arteriosclerosis.
8	F	40	Swelling	Excision of costal cartilage	Yes	Lymph nodes	Sinus healed 7 months after admission, followed 10 5/12 years; has had no recurrence of sternum disease.
9	F	26	Pain	Aspiration and resection of sinuses	Yes	Chest wall Peritoneum	Followed 10/12 years; slight drainage persists from three pin-point sinuses.
10	M	56	Pain	Incision and drainage, and biopsy	Yes	None	Left at own request against advice; followed 12 7 4/12 years; no recurrence of disease at sternum; bedridden past 3 years.
11	M	46	Pain	Curettage	Yes	Spine	Still hospitalized; has open granulating sinus over manubrium, with purulent drainage.
12	F	1 1/2	Swelling	None	No	Finger Spine Lungs	Still hospitalized; sinuses are healed.

berculosis of the ribs and costal cartilages.<sup>3</sup> Tuberculosis may also involve the lymphatic vessels situated in the anterior costal interspaces, as well as the internal mammary or sternal lymph nodes, and necrotic nodes in this area may give rise to abscesses. In female patients, tuberculosis of the breast must occasionally be considered. The injection of a radio-opaque substance under such circumstances readily gives the clue to the actual process. A negative tuberculin test helps to distinguish chronic nontuberculous osteomyelitis of the sternum from tuberculosis and is therefore of value. Syphilis can be identified by the Wassermann test and by the fact that syphilitic lesions usually heal rapidly with specific treatment. Sar-

In 25 per cent of the cases, the tuberculosis of the sternum became arrested spontaneously and the sinuses healed. In the remaining 75 per cent, a variety of operative procedures were performed, such as aspiration, incision and drainage, curettage and the resection of sinuses. Since these operations were performed by different surgeons in different hospitals, accurate evaluation is difficult. Aspiration was performed in 3 cases, in two of which further operation was unnecessary; in the third, resection of sinuses was performed later. Herrick<sup>1</sup> also reported a patient in whom aspiration was performed and whose lesion healed under conservative treatment. In the other cases, incision and drainage were done at least four times

restless,  $\frac{1}{2}$  gr and, 30 minutes later,  $\frac{1}{2}$  gr of morphine were given subcutaneously, with very little effect. During the afternoon he continued to be very restless, and uncooperative, whereas he ordinarily behaved well. In the late afternoon he began to vomit and hiccough and he continued to vomit during the next 36 hours. At 9:00 p.m., 2 gr of luminal sodium was given intramuscularly with no effect. At 11:00 p.m., the mistake in the strength of the solution not having been discovered, 10 gm of sodium sulfapyridine was given intravenously.

On November 29, restlessness became even more marked, and at 2:00 a.m. another 2 gr of luminal sodium was given intramuscularly. At 4:00 a.m., 1 cc of paraldehyde was given intravenously in an attempt to quiet the patient, but was absolutely without effect. At 7:00 a.m., 30 cc. of paraldehyde was given by rectum with slight sedative effect. At no time were convulsions or gross muscular twitching observed, and the patient was always clear mentally. He stated that he could not lie still. At 7:30 a.m., it was noted that the urine was dark and smoky. Examination of this specimen showed it to contain innumerable red cells and acetyl sulfapyridine crystals. Since a sample of serum contained no hemoglobin, no acute hemolytic process was present. During the morning the error in dosage was discovered and large amounts of intravenous fluids were started. During the next 24 hours, the patient received 6500 cc. of 5 per cent dextrose in distilled water, and 1000 cc of 5 per cent dextrose in saline. The urine continued to be grossly bloody but he voided 1560 cc.

On November 30, during the early morning hours the patient began to feel better and slept intermittently. The vomiting had ceased, although he was still somewhat nauseated, and the restlessness had largely disappeared. During the 24 hours he received 2500 cc of 5 per cent dextrose in distilled water and 1000 cc of 5 per cent dextrose in saline. The urine output was 3100 cc. In the afternoon, the urine was no longer grossly bloody, although microscopic blood was still present. On December 1 the major complaint was lower abdominal pain, which was relieved by bladder irrigations of distilled water. It was thought that the discomfort was due to a chemical cystitis. This pain gradually subsided during the next few days.

On December 3 moderate jaundice was first noted and the patient complained of some right upper quadrant pain. The lungs were clear. After the administration of sulfapyridine, the temperature had not risen over  $101^{\circ}\text{F}$  and over the course of several days it gradually fell to normal. Because of the jaundice, he was given intravenously 2000 cc of 10 per cent dextrose in distilled water daily for the next 5 days.

The jaundice gradually subsided and was not visible on December 10. No leukopenia, significant fall in the number of granulocytes or drop in hemoglobin occurred. Improvement was steady, and the patient was discharged on December 17 feeling quite well.

On February 29, 1941, he was seen by one of us (F.B.C.) and reported that he was feeling fairly well but had not yet regained full strength. Physical examination was negative. No jaundice was evident and the liver edge could not be felt. A complete blood examination

was entirely negative. A urine specimen had a specific gravity of 1.025, and was negative for sugar and albumin. Microscopic examination of the sediment, after centrifuging, revealed no casts or red cells. Two to four white blood cells per high power field were present, probably the result of a low grade bladder infection following the previous bladder irrigations. Chemical examination of a portion of the urine specimen for sulfapyridine was negative. The blood urea nitrogen was 13 mg per 100 cc.

In Figure 1 some of the laboratory findings are charted. Unfortunately, no blood was taken for drug determination until 10 hours after the second intravenous dose. At that time there was still 207 mg of free and 290 mg of total sulfapyridine per 100 cc of blood. The method employed

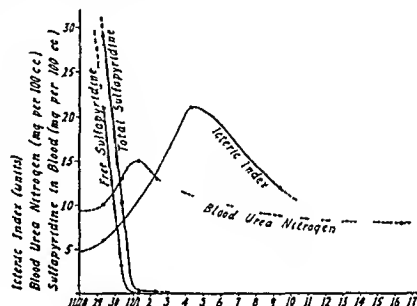


FIGURE 1

was that of Bratton and Marshall,<sup>3</sup> using a 1:75 dilution of the blood, after standardization for sulfapyridine on the Cenco photometer. The free drug had been excreted 57 hours after the last administration, although traces of acetyl sulfapyridine were still present 81 hours after the second dose.

### SUMMARY

The patient in this case, suffering from post-operative pneumonia, received, through an error, 30 gm of sodium sulfapyridine intravenously in a ten hour period. He survived probably because of his youth, good kidney function and the prompt administration of large amounts of intravenous fluids. Convulsions, muscular twitching and anuria were not observed, but marked restlessness and irritability, gross hematuria and jaundice were strikingly evident.

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## GUMMA OF THE FRONTAL BONE

## Report of a Case

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**F**EW general practitioners who have occasion to treat late syphilis have an opportunity to watch a definite lesion clear up dramatically under treatment. Frequently the wisdom of intensively treating such cases is questionable, in view of reactions. The following case of gumma of the frontal bone completely resolved under antisyphilitic therapy that could by no means be called intensive. Furthermore, it illustrates that the titer of

skin edges were widely undermined to the mid forehead, beyond the hairline, to the zygomatic arch and into the upper lid. The temperature, pulse and respirations were normal. Examination of the urine was negative. Hospitalization was advised and promptly refused. A blood serologic test, culture and biopsy, suggested as an alternative, also met with refusal. The patient insisted that all he wanted was "some salve and something for the pain." Believing that he might possibly feel differently later, I applied zinc peroxide paste to the lesion; codeine was prescribed for the pain, and the patient was told to

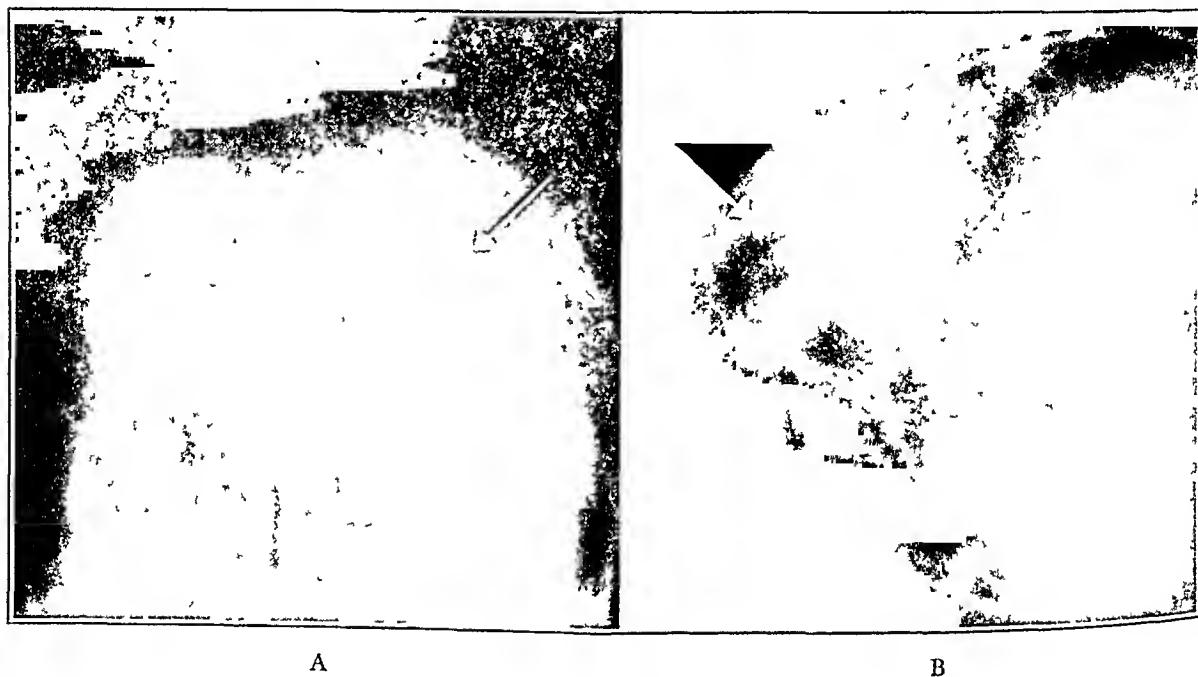


FIGURE 1. X-Ray Films Taken March 4, 1938.  
A is the anteroposterior view; and B, the lateral.

a serologic test for syphilis may remain exactly the same in spite of a dramatic clinical result.

## CASE REPORT

G.D., a gas-station attendant, had first consulted a physician on December 25, 1937, because of pain and swelling in the right forehead after a glancing blow several days previously. Hot compresses were advised, and 24 hours later the area was incised. According to the patient, "quite a lot of pus came." The lesion was dressed daily, but evidently became progressively worse.

I was first consulted on February 4, 1938. At that time, a draining, ulcerated lesion about the size of a half dollar was found just above the right eye. The upper right lid was edematous, and the eye was completely closed. Bare bone could be detected at the base of the ulcer. The

return on the next day. However, he did not return until March 4.

In the meantime, the pathologic process had gone from bad to worse. Practically the entire right forehead had become ulcerated, and the pain was intense. The temperature, pulse and respirations were still normal. Although the patient continued to refuse hospitalization, he agreed to permit certain procedures. X-ray films of the right frontal region and blood for a serologic test for syphilis were then taken. Smears of the lesion were negative for tubercle bacilli. The patient was placed on 15 gr. of potassium iodide empirically, the lesion was cleansed, and a dry sterile dressing was applied. The test for syphilis was reported as positive in a titer greater than 1:10. The x-ray films (Fig. 1) were reported as follows by Dr. James W. Walton, of the Horton Memorial Hospital:

Radiographic examination reveals an area of disease in the right frontal bone extending down to the zygomaticofrontal suture, backward almost to the frontoparietal suture and medially almost to the mid line. The lesion is approximately 7.5 cm in diameter, with densely sclerosed edges and an area of rarefaction in the center measuring at least 2.5 cm in diameter. This area is very circumscribed and has very densely sclerosed edges, and because of its location, could be a gumma. If a definite history of injury some time ago can be obtained, chronic osteomyelitis must be considered, but there is more sclerosis than is usually seen in this condition.

The dose of potassium iodide was immediately increased to 30 gr, and protoiodide of mercury was administered in

Clinically, the lesion had entirely healed with the exception of a small area about 3 mm in diameter. This cleared up about 2 weeks later.

Treatment was continued until July 30, but during the entire course of the disease the patient received only ten injections of Mapharsen and eleven of Bismarsen. Repeated serologic tests for syphilis remained positive, with a titer greater than 1:10.

The patient was seen on March 1, 1940, for another complaint, and at that time, with the exception of a barely noticeable amount of puckering, nothing remained of the original lesion.

Although not many cases of gumma of the frontal bone have been reported, the lesion is



A

B

FIGURE 2 X-Ray Films Taken June 17, 1938  
A is the anteroposterior view and B, the lateral

doses of  $\frac{1}{4}$  gr three times daily. Within 48 hours, the pain was relieved. On March 9, the patient was started on small doses (0.2 gm.) of Bismarsen. Mapharsen was instituted on March 24.

The x-ray report on April 18 was as follows:

Radiographic re-check of the right frontal bone shows very extensive resolution of the area of sclerosis with central destruction—apparently a gumma—previously reported. The smaller areas previously reported also show considerable resolution.

The clinical appearance of the lesion had also been markedly changed. The edema of the right upper lid had disappeared, the drainage had ceased, and granulation tissue had appeared. Most important of all, the soreness had entirely disappeared. Antisyphilitic therapy was continued, with a shift to 0.2 gm. doses of Bismarsen on June 6, but only dry sterile dressings were applied to the wound.

The last x-ray films (Fig 2) were taken on June 17, and were reported as follows:

Radiographic re-check of the right frontal bone shows complete resolution of the area referred to in previous examinations (Fig 1). There is moderate bone sclerosis in this area.

not generally considered rare. Most patients seem to do well, but complications occur in the underlying structures, and deaths have been reported. In the diagnosis, the most important feature is to think of the possibility of and to take a specimen for a serologic test for syphilis in all open lesions. This case is of further interest in that the therapy was not too intensive because the patient would not co-operate, the blood titer remained unchanged, and yet the lesion responded dramatically.

#### SUMMARY

A case of gumma of the frontal bone is presented, and the importance of serologic tests in all such open lesions is stressed. Antisyphilitic therapy brought about complete resolution of the lesion, even though the serologic titer remained exactly the same.

## MEDICAL PROGRESS

## NEUROLOGY

JAMES B. AYER, M.D.\*

BOSTON

VITAMIN E AND CERTAIN DISEASES OF THE  
NERVOUS AND MUSCULAR SYSTEMS

**T**WO diseases have come into prominence during the last two years because of possible successful treatment by vitamins, and especially by vitamin E: namely, amyotrophic lateral sclerosis and progressive muscular dystrophy.

Before the effect of treatment is discussed, a few words about diagnosis are in order. Progressive muscular dystrophy is generally considered a slowly progressive disease in which muscle-fiber wasting is the prime factor, and replacement by fat a secondary manifestation. No causative lesions are found in the central or peripheral nervous system. In the typical advanced case, there is little difficulty in making a diagnosis; in the early stages and in atypical cases, diagnosis is often in doubt for months or years. Amyotrophic lateral sclerosis, when conforming to the original Charcot description, is a disease of the spinal cord in which the latter shows, anatomically, degeneration of the anterior-horn cells and pyramidal tracts bilaterally, with no evidence of inflammation, compression or vascular disturbance. Clinically, the patient shows weakness, with atrophy of the muscles, usually beginning in the hands, and spasticity, usually beginning in the legs; the two processes relentlessly extend in intensity and in parts involved, and end in bulbar palsy.

Amyotrophic lateral sclerosis in its early stages and even later also simulates a number of other conditions, so that most neurologists advisedly make the diagnosis of "amyotrophic lateral sclerosis syndrome." Later developments show that a large number of these patients do not run the course of the typical Charcot description. Rubenstein<sup>1</sup> has recently emphasized this point: of 8 cases studied, only 4 were typical; the other 4 afforded evidence that somatic disease caused a clinical picture similar to that of the disease under consideration.

The difficulties in diagnosis must be kept constantly in mind before one accepts at face value the results of treatment in these two diseases. And

yet it is fair to say that when the clinical picture is such that either diagnosis has been seriously entertained, the outlook for recovery is not good, and any agent that will arrest the process should therefore be welcome, whatever the exact diagnosis.

In 1939, at the International Neurological Congress at Copenhagen, a paper by Einarson and Ringsted<sup>2</sup> on vitamin E stimulated interest. They observed atrophy and spinal-cord degeneration in rats as a result of vitamin E deficiency. In 1940, Bicknell<sup>3</sup> published a paper reporting such encouraging results in dystrophy that he makes this bold statement, "The discovery of the importance of vitamin E in the treatment of muscular and nervous diseases appears to be revolutionary." He claims improvement in 12 cases of progressive muscular dystrophy out of 13 treated for six weeks or more. Of 4 cases of amyotrophic lateral sclerosis, 2 were improved, and 2 died with bulbar paralysis. His treatment was 15 gm. of dried whole-wheat germ twice daily by mouth. His case reports are meager, frequently only a few lines, and improvement was often admittedly dependent on report rather than personal evidence. On the basis of evidence given, it is difficult for one to reach the optimistic conclusions quoted above. Stone<sup>4</sup> is also encouraged by treatment of pseudohypertrophic muscular dystrophy and of myotonia congenita. Wechsler<sup>5, 6</sup> undoubtedly is chiefly responsible for stimulating interest in vitamin E in the United States. In his later paper, he analyzes 20 of his 30 cases of amyotrophic lateral sclerosis. He admits a difficulty in diagnosis but believes that vitamin E is especially successful in the degenerative type. He used alpha-tocopherol acetate by mouth, up to 50 mg. daily, and intramuscular injections of this drug in oil; he also gave 2 teaspoonfuls of wheat-germ oil by mouth. Vitamin B complex and a vitamin-rich diet were also given. Two patients recovered, 4 showed marked improvement, and 6 improved somewhat.

A number of other papers on this subject have been published during the past year, some strongly in favor, others giving negative results of treatment. Papers written from four large clinics—Cornell, Columbia, Mayo and Harvard—uni-

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formly show poor therapeutic results. Denker and Scheinman,<sup>7</sup> using even larger doses of vitamin E than those recommended by Wechsler, assert, on the basis of 15 patients, that "no therapeutic results of any value were observed." Ferree et al.<sup>8</sup> state that "vitamin E and vitamin B<sub>12</sub> preparations, given in large amounts, failed to influence the course of either amyotrophic lateral sclerosis or muscular dystrophy in a series of patients followed for a period of two to twelve months." Workers at the Mayo Clinic<sup>9</sup> and at the Neurological Unit of the Boston City Hospital<sup>10</sup> are likewise unimpressed.

At a meeting of the Boston Society of Psychiatry and Neurology in April, reports were made from the Boston City and Massachusetts General hospitals, and the conclusions reached and the discussion were pessimistic. However, in chronic diseases, with the diagnostic difficulties mentioned earlier, one should not judge too quickly a therapy that has the support of men of the standing of Wechsler.

The best results have been obtained in the treatment of dystrophy in children; the worst results have been in cases of bulbar palsy. Another year should determine the value of this form of treatment.

#### BASILAR ANOMALIES AND THE ARNOLD-CHIARI MALFORMATION

For many years, malformations of the occiput, atlas and axis have been recognized as interesting anomalies. Knowledge of the displacement of medulla, cerebellum and spinal cord, commonly known as the "Arnold-Chiari malformation," goes back to 1894 and 1895.

Recently, there have been attempts to establish a relation between these anomalies, one of bony development, the other of the central nervous system. Although the two conditions occur independently of each other, there appears to be a developmental relation. The symptomatology is similar enough to include both conditions in comparative discussion. To be thoroughly inclusive in a clinical differentiation at this level, one should also consider syringomyelia and high cervical-cord tumor.

An extremely lucid and well-illustrated paper on the bony anomalies of this region is that of List.<sup>11</sup> He explains the anomalies on a basis of abnormal fetal development and incorrect ossification, with subsequent modification by rickets, weight bearing and so forth. He recognizes in his cases four types of deformity: malformation of the occipital foramen and basilar impression (platybasia); fusion of the atlas with the occiput

and malformation of the atlas; fusion of other cervical vertebrae and malformation of these vertebrae; and abnormal position of the axis in relation to the occiput and atlas. These anomalies may be considered essentially benign, but with continued growth and under stress, neurologic symptoms may arise. The chief interest concerns platybasia, in which the basiocciput is thinned and mushroomed upward by the atlas, and the foramen magnum is narrowed. The medulla resting on this floor is thus compressed anteriorly and constricted in its passage through the narrowed foramen magnum. The neurologic picture is naturally one of medullary compression, and when the fluid pathways become obstructed, of super-added hydrocephalus. If in the advance of the process, dislocation of the axis on the atlas occurs, upper cervical-cord symptomatology is to be expected.

The Arnold-Chiari deformity concerns the nervous system. The medulla and cerebellum are displaced downward through an enlarged foramen magnum into the cervical canal. In the case reported by Penfield and Coburn,<sup>12</sup> the cerebellum extended to the third cervical vertebra. Such a displacement leads to medullary jamming in the foramen magnum, with extreme traction on the lowest cranial-nerve roots and with cerebellar symptoms, and additional symptoms of increased intracranial pressure. The mechanism by which this downward herniation of the brain through the foramen magnum occurs is not always clear, but in Penfield's case it was satisfactorily explained as follows: in childhood, the patient had been operated on for a mid-dorsal meningocele; at autopsy, the dura and consequently the spinal cord and nerve roots were firmly adherent at the point of operation. It seemed apparent that this attachment prevented the normal ascent of the cord in the spinal canal with growth, and consequently the upper portions of spinal cord, medulla and cerebellum were slowly drawn down. This mechanism is probably not the only possibility in explaining the downward displacement, for in some cases there is no meningocele. Adams and his associates<sup>13</sup> have studied a case of this type, without evidence of meningocele. An operative decompression so completely relieved the symptoms that the patient returned to work.

Although points of clinical differentiation are made between platybasia and the Arnold-Chiari malformation, both conditions produce slow pressure on the medulla, cerebellum and low cranial nerves, and both conditions must be considered in lesions that indicate an abnormality near the foramen magnum. Furthermore they must be differen-

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bilateral frontal trephine openings, the cerebrospinal-fluid pressure being lowered by lumbar puncture to facilitate the filling of the subdural space. An x-ray film showed clearly a tentlike projection of tissue, which prevented air filling in the left postfrontal region. This was subsequently found to be scar tissue and was removed at operation, with cessation of attacks.

It is of course well known that convulsions are a frequent accompaniment of brain tumor. That epilepsy may be the first symptom of tumor is likewise recognized. But it will come as a surprise to many that, in two types of brain tumor,—astrocytoma and meningioma,—seizures occur as the first symptom in 60 per cent and 62 per cent respectively. The figures are from the Montreal Neurological Institute.<sup>21</sup> It is interesting to note that these types of tumor are the two that are most frequently operable; furthermore, the tumors are encapsulated and near the surface of the brain. The obvious deduction from this paper is that a patient with late epilepsy must be considered a "brain-tumor suspect" and every effort made to confirm the diagnosis.

Although uncommon in the United States, cysticercosis as a cause of epilepsy should not be forgotten, particularly in view of the accuracy of diagnosis. The question should always be considered in any patient returning from the Orient. Dixon and Smithers<sup>22</sup> speak of epilepsy, generalized or jacksonian, as frequently occurring in this disease. The brain cysts may or may not be calcified. The diagnosis is made presumptive when large numbers of calcified organisms in the skeletal muscles are revealed either by palpation or by x-ray study.

Ray<sup>23</sup> has recently published a case report of especial interest because of the satisfactory outcome following surgery. The patient evidently became infected in India; the diagnosis was correctly made in 1936 in England on the basis of convulsions and the demonstration of calcified cysticerci in the muscles. Presumably because brain metastasis is often multiple, surgery was not offered at that time. Soon after, Ray successfully removed a solitary cyst from the parietal cortex and confirmed the diagnosis histologically. The patient was said to be well and working, four years after operation.

#### FRONTAL ASSOCIATION AREAS AND OPERATIONS ON THEM

Because the frontal lobes are phylogenetically new and well developed in man as compared with any lower animal species, it is reasonable that they should have been considered the seat of in-

tellect. That this is only partially true is becoming evident, as studies on apes and most significantly on man himself are beginning to reveal. Since operative procedures on this region are now designed with increasing boldness, it is well to consider what is already known.

It is necessary to distinguish the anatomic frontal lobe from the frontal association areas. The posterior portion of the frontal lobe is bound up with motor function, posture, speech and eye movements, and the anterior portion, which is histologically different, has no direct control over these functions. The latter areas, which are so well developed in man, are the regions under consideration: the frontal association areas.

Physiologic evidence of function of these areas, as abstracted from Fulton's<sup>24</sup> work, is as yet not great and not too certain. He states:

The frontal areas are inexcitable to all forms of electrical stimulation and their primary ablation has little if any effect upon reflexes or posture of the extremities in any primate form including man. . . . Unilateral ablation . . . causes no obvious behavioristic disturbance in monkey, chimpanzee or man; but their bilateral destruction leads to a conspicuous syndrome characterized in animals by restlessness, distractibility and failure of immediate memory.

He cites Jacobsen's experiments with apes; these indicate that bilateral ablation appears to show that recently acquired experience could not be assimilated and utilized in problems that were readily solved by the same animals before operation or after unilateral frontal ablation. Jacobsen's experiments with conditioned reflexes were most interesting. When balked, the normal animal became frustrated to a degree approaching neurosis. After bilateral frontal ablation, the same mistakes called forth little or no emotional response. The animal was restless and distractible but presented the "fatuous equanimity of spirit which one encounters in a good-natured drunkard."

Because the frontal association areas are preeminently well developed in man, it is probable that their function will be revealed by studies on man. There is general unanimity of opinion that unilateral ablation or destruction fails to show clinical evidence; neither abnormal performance nor lack of it can be recognized by present methods. Although a tumor of one frontal lobe may be accompanied by personality changes, close analysis invariably discloses the certainty that no abnormality existed until the tumor had expanded sufficiently to implicate the other frontal lobe by pressure or by invasion of the corpus callosum. I have recently had a clear-cut demonstration of this point in a nineteen-year-old girl who at fifteen years of age had had a convulsion. X-ray ex-

amination of the skull at that time showed a definite deposit of calcium in the tip of the right frontal lobe. Since no other symptoms and no further attacks of epilepsy appeared, the patient continued her studies, was admitted to college, and was considered a normal girl in every way. Only when headache supervened five years later, with evidence of increased intracranial pressure, did her intellectual output suffer, together with an alteration of personality of which distractibility, facetiousness and punning were outstanding. At operation, Dr. W. Jason Mixter was obliged to resect the right frontal lobe up to the premotor area because of an invasive tumor, probably an astrocytoma.

Almost every physician will probably recall at least one patient with a small lesion of one frontal lobe, whether from tumor, trauma or abscess, that gave no hint of its presence until sufficiently large to alter the function of both frontal lobes. Jefferson,<sup>25</sup> on the basis of 8 unilateral frontal lobectomies, states: "Those who showed no mental alteration before the operation were unaffected by partial removal of the anatomical frontal lobe . . . those who had mental symptoms [because bilateral function was presumed to be affected] were much better after the lobe had been excised." Nor did Jefferson and other authors find evidence for right or left frontal-lobe dominance if the lesion was confined to the prefrontal region.

In a discussion of frontal-lobe symptoms, bilateral involvement of the frontal association areas is therefore implied. To most observers, the character changes as represented by the general parietic come first to mind; others remember the personality traits of Phineas Gage, whose frontal lobes were largely destroyed by a crowbar.<sup>26</sup> The placard accompanying the skull and bar in the Warren Museum reads, "His disposition was noted to change but in minor ways: he became fitful and vacillating, profane and obstinate, which was different from what he had been before the accident, but no other deviation was noted."

But neither of these examples can safely be depended on as evidence that personality traits reside in the frontal lobes. Nor can one say that the frontal lobes act as a brake on the restlessness, the emotional instability, the joking and the obscenity of such a patient. Brickner<sup>27-29</sup> has made what is probably the first and most extensive study of an appropriate case, a man in whom Dandy removed both frontal association areas because of a tumor (meningioma) confined to this region. The objective characteristics of this man, which continued unchanged from the operation in 1930 to the last report in 1939, were not greatly

different from those of Phineas Gage. The patient was emotionally unstable, a braggart, a wife-baiter and a silly punster, and he was often vulgar and obscene. His mental processes were not deficient, but he showed intellectual inertia. His wife stated that his postoperative traits were not different from what they had been before, but that they were intensified. After thorough psychological tests, Brickner concludes that this array of unproductive traits is the result of a "diminution in the amount of synthesis, which places a limit upon the degree of attainable complexity of thought."

Hebb and Penfield<sup>30</sup> report on bilateral frontal lobectomy in a man presenting post-traumatic epilepsy and a personality change to the extent that he had "become a behavior problem—irresponsible, childish stubborn, restless and forgetful." Following the operation, convulsions were reduced to a minimum, intelligence improved, as shown by specific tests, and behavior was now socially acceptable. The authors are unwilling to commit themselves about the extent to which the frontal association areas influenced the behavior of this man: "It may be that no laboratory study will be adequate to reveal whatever defects follow frontal injury in man because of insufficient control of environmental factors and the difficulty of obtaining a good premorbid rating of ability."

It therefore seems possible to produce certain changes of behavior and disturbance of intellectual balance by partial destruction of the frontal lobes, and also to bring about improvement in behavior and intellect by ablation of the same areas. This brings us to the crucial experiment, usually only possible in the physiologic laboratory, but now practiced on man for therapeutic purposes, that is, bilateral frontal lobotomy on the normal cortex. In this country, Freeman and Watts<sup>31</sup> have been the pioneers in this operation, which consists in cutting the nerve-fiber connections of the frontal association areas: "The white matter in each frontal lobe is cut just anterior to the tip of the ventricle in the plane of the coronal suture." This operation on man may be considered to be based on the observations of Jacobsen on apes, mentioned above, and is used for its stabilizing effect on cases of agitated depression.

Excerpts of three stages of the effects of the operation will give an impression of the results to be expected:

The patients can converse quite rationally during the operation upon either the right or the left side of the brain, but often as soon as the first incision is made in the frontal lobe on the opposite side, there is immediate abolition of anxiety and nervous tension; the pulse and blood pressure fall within a few minutes

the skin of the extremities becomes warm and flushed, and there is considerable sweating. As the incision into the white matter is made more extensive, the patient becomes disoriented, and with the final incision, upward or downward, becomes drowsy or goes into stupor from which he is roused with difficulty and answers in monosyllables.

During the following two or three days or longer, there is vesical incontinence, and the sluggish state persists. Neurologic signs other than these are usually absent. The physical condition remains good. The patients are often restless and try to get out of bed, and upon questioning are found to be completely disoriented. These patients present a placidity and indifference that forms a striking contrast to their previous apprehensive state.

When examination is carried out 7 months after operation, it is found that there is a certain inertia present. The patient responds courteously and accurately, but volunteers little. The relatives state that the patient spends most of his time sitting in a chair, not reading or playing games, apparently perfectly at ease but merely unoccupied. The patients make plans for tomorrow, but somehow, tomorrow never comes. They do enough for today, and then stop. On the other hand, if given a task of more or less repetitive character, they will often continue more or less automatically, beyond the limits of normal patience.

As an antidote to the distressing symptoms presented by a patient who is agitated and depressed, the remote effects of frontal lobotomy as above quoted are very welcome both to the patient and to his relations. The operation restores him to society, but not to competitive occupation. This fortunate outcome has been brought about in a patient known to me whose case was recently reported by Mixer and Tillotson.<sup>32</sup> The patient had remained unchanged for seven years in an institution, but for two years since operation has lived comfortably at home.

There is no clear answer to the question, What is the function of the prefrontal lobes or the frontal association areas? Brickner believes that these areas "synthesize" sensory impressions, Freeman and Watts believe that "they assemble the available data, synthesize them, plan a course of action with the idea in mind, and, equipped with energy of response and with appropriate affective tone, project the individual into the future, direct him toward his goal—and criticize his shortcomings." It also seems probable, as intimated by Hebb and Penfield, that these areas exert a control over psychologic processes that varies with the patient's previous intellectual and emotional life and the social environment in which he lives.

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 27381

#### PRESENTATION OF CASE

A fifty-seven-year-old Italian woman entered the hospital complaining of vomiting of two weeks' duration. Because of the patient's condition, the history was obtained from her husband.

Seven years before admission, the patient visited her physician, complaining of pruritus, weakness and restlessness. A diagnosis of diabetes was made, and she was put on a diet without insulin.

She carried on until six months before admission, when for unstated reasons she saw another physician. He found that the urine contained a large quantity of sugar, boiled solid with albumin, and was full of red cells and casts. At this time, an oculist noted that the fundi showed "a combination of diabetic and albuminuric retinitis." Protamine insulin was now used in doses of 40 units twice a day. Three months later, the patient developed what appeared to be bronchitis, with a chronic cough and white sputum, began to lose weight rather rapidly, and suffered from weakness, headaches, dizziness, dyspnea and ankle edema. The symptoms progressed, and two weeks before admission anorexia and vomiting appeared and she became drowsy and listless. Her physician heard wheezes throughout her chest and recorded a blood pressure of 160 systolic, 90 diastolic. Digitalis was given, but since the vomiting grew worse, it was discontinued.

In the preceding few days, the family had noticed that the patient's speech and behavior were peculiar. At the time of admission, she was nearly blind, had lost 60 pounds in the previous six months, and had complained of frequency and a nocturia of once a night for some time.

At no time had there been pain, orthopnea, hemoptysis, hematuria, gravel, chills, fever, convulsions or localized weakness. Vomiting had ceased five days before entry.

The past and family histories were irrelevant.

On examination, the patient was in no acute distress, but irrational and very unco-operative. The ears, nose and throat were normal; the fundi were not seen. The heart was markedly enlarged

to the left, with a gallop rhythm and an apical systolic murmur; the blood pressure was 210 systolic, 110 diastolic. Moist rales were heard at the lung bases. The liver was palpable two finger-breadths below the costal margin, the abdomen being otherwise normal. Examination of the nervous system was negative, so far as it could be studied.

The temperature was 100.5°F., the pulse 120, and the respirations 25.

The urine ran a specific gravity between 1.008 and 1.015, with a ++++ test for albumin. The blood showed a red-cell count of 4,000,000 with 135 gm. of hemoglobin (photoelectric-cell technic), and a white-cell count of 6500. The nonprotein nitrogen of the blood serum was 38 mg. per 100 cc., the sugar 151, the protein 6.4 gm. per 100 cc.; the chlorides 99.8 and the carbon dioxide combining power 25.9 milliequiv. per liter. The stools were guaiac negative.

An x-ray film of the chest showed the heart to be enlarged in the region of the left ventricle. The lung fields were clear, and the aorta was not remarkable.

With an intravenous pyelogram, the size of the kidneys was in the upper limits of normal. No unusual areas of calcification were seen in the region of the kidneys, but multiple areas of calcification were present in the left side of the pelvis (probably phleboliths). Only traces of dye were visible in the kidney pelves, incompletely outlining them over a course of sixty minutes. Nothing could be said about the shape of the kidney pelves.

The patient was digitalized and given 40 units of protamine insulin daily, the urine remaining sugar free. There was a general improvement for a short time, but she remained disorientated, irrational and sometimes unruly. On the sixth hospital day, the nonprotein nitrogen was 40 and the sugar 140 mg. per 100 cc.; the carbon dioxide combining power was 20.8 milliequiv. per liter. The following day, a flaccid paralysis of the right arm and leg accompanied by aphasia suddenly developed and she was unable to take nourishment. The patient then became comatose, responding only slightly to painful stimuli.

Ten days after admission, tubular breathing and coarse rales were present in the right lower lobe, the temperature rose to 105°F., and the patient vomited occasionally.

Death occurred the next day, the temperature rising terminally to 108°F.

#### DIFFERENTIAL DIAGNOSIS

DR. JOHN H. TALBOTT: This abstract describes the medical history of an Italian housewife who

had suffered from diabetes mellitus for seven years, and from vomiting and mental disorientation for two weeks. The diabetes was presumably mild during the greater part of the period, for no insulin was necessary until six months before admission. The first evidence that something was wrong with the kidneys appeared during a routine examination for urine sugar. It was noted that the specimen boiled solid, probably because of the high albumin content. Examination subsequently revealed red blood cells and casts in the urinary sediment. Examination of the eye grounds showed diabetic and albuminuric retinitis. There is no mention of papilledema of the nerve head, and we can assume that there was not a significant increase in intracranial pressure.

The onset of the present illness may be dated by this examination. The need for 80 units of protamine insulin per day for a patient receiving none previously is significant. I have assumed from this observation that a complication of diabetes mellitus or some new malady was responsible. The story of a weight loss of 60 pounds confirms this assumption. Yet there were no clinical symptoms until three months before entry. The appearance of a chronic cough and white sputum suggested a pulmonary process, and the diagnosis of bronchitis was made. Symptoms of weakness, headache, vertigo, dyspnea and ankle edema then divert our attention from the lungs and center it on the cardiovascular-renal system.

The patient was admitted to the hospital because of vomiting and mental disorientation. I presume we can exclude a brain tumor, because the statement is made in the record that convulsions and localized weakness were looked for but not observed. Furthermore, if an expanding lesion of the brain were responsible for the cerebral symptoms, I should not expect vomiting to cease spontaneously. There is no further information about the eye grounds at the last admission, except that they were not visualized. No mention is made of the flexibility of the neck, and I assume it was not rigid. A gallop rhythm suggests that the heart was functioning at a disadvantage. The apical systolic murmur, enlargement of the heart by x-ray examination and the blood pressure of 210 systolic, 140 diastolic are indicative of further strain on the myocardium.

We have ample evidence of a renal dysfunction. The presence of large amounts of albumin was observed for at least six months. The maximum specific gravity of the urine was 1.015. It is not stated whether the maximum specific gravity was observed during a so-called "urine-

concentration test," or whether this represented the maximum of several casual specimens. Recently, we have been helped by a new test for determining maximum urine specific gravity. The test needs less preparation than the other tests recommended and is probably more accurate. Without previous preparation, the patient is given 0.5 cc. of surgical pituitrin subcutaneously. Half-hourly urine collections are made for three hours, and the volume and specific gravity recorded. A normal person should concentrate to 1.020 during the test.

Turning again to the patient under consideration, it is reported that the nonprotein nitrogen was 38 mg. per 100 cc. and that the serum protein was 6.4 gm. per 100 cc. I believe that the patient was dehydrated on admission, and that this value if corrected for dehydration would be somewhat below normal. The serum chloride, carbon dioxide content and blood sugar were essentially normal. These concentrations do not permit us to make a diagnosis of diabetic acidosis and coma. X-ray studies showed normal lung fields. The intravenous pyelogram showed incomplete outlines of both kidneys, which were at the outer limits of normal in size. No abnormal calcification was seen.

During observation on the ward, the patient was digitalized, with some benefit. Paralysis of the right arm and right leg developed, however, and death followed, with a temperature of 103°F.

In summary, we can say that the patient had diabetes mellitus as well as hypertension. There was hypertrophy of the heart and cardiac decompensation. These diagnoses are given to us in the history.

The matters that we have to decide concern the precise nature of the renal disturbance and the pathogenesis of the cerebral symptoms. With the evidence given, we are entitled to be suspicious of a brain tumor, cerebral abscess, subdural hematoma and tuberculous meningitis. There is not sufficient evidence, however, to implicate any one of these specifically. If we rule out each of these cerebral conditions as being responsible for vomiting, and have no gastrointestinal studies to suggest a peptic ulcer or a neoplasm, it is reasonable to attribute the vomiting to chronic renal insufficiency. The remaining cerebral symptom to be explained, namely hemiplegia, can best be attributed to a vascular accident. Because of the frequent association of hypertension and hemiplegia, I should favor a cerebral hemorrhage.

The renal lesion is even more intriguing. I do not believe that this is a case of the usual variety of acute nephritis, nor am I concerned about the

diagnosis of nephrosis. It is true that most of the clinical findings could be explained by a diagnosis of chronic nephritis, but somehow it does not impress me as being the ordinary variety of chronic nephritis and uremia. This leaves us with but one choice. There is a particular type of kidney lesion observed frequently in patients of this age group suffering from diabetes mellitus and hypertension. The lesion is characteristically confined to the intercapillary spaces. I think it reasonable to believe that this patient had anatomic involvement of the intercapillary spaces, because from 15 to 30 per cent of well-studied autopsied cases of patients with diabetes mellitus and hypertension have such a renal disease.

DR. EARLE M. CHAPMAN: You believe that the lesion shown at autopsy will probably be intercapillary glomerulitis, the type that Kimmelstiel and Wilson<sup>1</sup> reported from the Mallory Institute.

DR. TALBOTT: On the law of probability, I should favor such a diagnosis.

DR. ALLEN G. BRAILEY: Do you not think it is fair to assume that this goes back much longer than six months?

DR. TALBOTT: I doubt if the patient had massive albuminuria for three years.

DR. F. DENNETTE ADAMS: On the ward, we were at first unable to account for the mental picture. When the paralysis developed, we made a diagnosis of cerebral thrombosis rather than hemorrhage, and believed that the mental symptoms could be best explained on the basis of a progressive vascular lesion, which first affected a silent area. We expected that the brain at post mortem would show a large area of infarction.

DR. TALBOTT: It might be of interest to mention the findings of one hypertensive patient examined in this department. The patient had symptoms typical of cerebral hemorrhage, an acute onset of paralysis, and at autopsy no evidence of acute hemorrhage or thrombosis was present. The patient had cerebral disease associated with malignant hypertension but no localized lesion.

#### CLINICAL DIAGNOSES

Diabetes mellitus.  
Hypertension.  
Hypertensive heart disease.  
Nephrosclerosis.  
Cerebral thrombosis.

#### DR. TALBOTT'S DIAGNOSES

Diabetes mellitus.  
Hypertensive heart disease.  
Cardiac decompensation.  
Cerebral hemorrhage.  
Intercapillary glomerulosclerosis.

#### ANATOMICAL DIAGNOSES

Cerebral thrombosis, left internal carotid artery.  
Cerebral infarction, left parietal lobe.  
Intercapillary glomerulosclerosis.  
Cardiac hypertrophy, hypertensive type.  
(Diabetes mellitus.)  
Arteriosclerosis, generalized, severe.

#### PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: At autopsy, this patient showed a thrombosis of the left internal carotid, with an infarct of the left parietal lobe. The heart was hypertrophied, weighing a little over 500 gm. The hypertrophy was for the most part left ventricular, characteristic of the hypertensive type. The kidneys were large, smooth surfaced and somewhat swollen, and at the time of autopsy a definite gross diagnosis could not be made. Microscopically, however, there is no doubt that this is the type of sclerosis within the glomerular tufts that was first described in 1936 by Kimmelstiel and Wilson,<sup>1</sup> the type associated with hypertension, diabetes and very often edema. Practically every tuft shows sclerosis and hyalinization of the connective tissue between the glomerular capillaries. The hyalinization occurs in the central portions of the glomeruli, leaving the peripheral capillaries open.

DR. TALBOTT: Are these cases all associated with diabetes?

DR. CASTLEMAN: I believe so. Recently, the clinical features of this syndrome have been more fully described by Derow and his associates<sup>2</sup> and by Newburger and Peters.<sup>3</sup>

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#### CASE 27382

##### PRESENTATION OF CASE

*First Admission.* A fifty-year-old man was admitted to the Medical Service complaining of cough with occasional blood-streaked sputum.

The patient was apparently in good health until seven years before admission, when he developed a severe cold, which confined him to bed for five days and to his home for one week longer. The cold was associated with a severe distressing cough, which caused him to raise occasional blood-streaked sputum. At times, he stated that he had coughed clots of dark-red blood. Following paroxysms of coughing, he occasionally vomited. Fol-



lowing this illness, he noted a persistent wheeze with respiration and a rather constant easy fatigability, malaise and general torpor. During the following six years before admission, he suffered frequent colds, usually in the "chest," which occurred mostly in the winter. With these colds, he experienced difficulty in breathing; he was required to sleep on at least two pillows because lying flat seemed to suffocate him. During this six-year interval, he had also what he described as chronic indigestion and the presence of a vague pain, sometimes sharp, usually associated with coughing and located in the region between the shoulder blades.

Physical examination revealed a thin, wasted, ill-developed man who coughed frequently. There was an acneiform eruption over the back. The teeth were dirty and carious, the chest was slightly asymmetric, and the upper half of the right chest appeared distinctly smaller than the left. There was a slight degree of lateral curvature of the spine. The breathing was described as "rough," and was somewhat prolonged in the expiratory phase. There were coarse musical rales throughout, and a few crepitant rales were audible at the right apex. The diaphragms descended moderately. The right external inguinal ring was slightly dilated. Rectal examination revealed the presence of hemorrhoids.

The temperature, pulse and respirations were normal.

Examination of the urine was negative. Examination of the blood showed a red cell count of 4,600,000 with 80 per cent hemoglobin, and a white cell count of 8600 with 75 per cent polymorphonuclears, 17 lymphocytes, 7 monocytes and 1 eosinophil. The smears were negative. The sputum was negative for acid fast organisms. The stools were guaiac negative. The blood Wassermann reaction was negative. X-ray examination of the chest revealed that the upper part of the right lung field was less radiant than the left. There was a rather dense shadow at the extreme apex. The hilar shadows were increased in size and density on both sides. The larger lung markings were prominent. Both apices were retracted. The patient remained in the hospital for eleven days and throughout the interval in a temperature that ranged from 98 to 99°F, pulse from 65 to 85 and respirations from 20 to 24. He was discharged to a convalescent hospital for chronic supportive care.

*Final Admission* (twelve years later). Since the patient's discharge, he had been in many hospitals for treatment of his chest troubles. He ceased

work two years before admission "because of his heart." One year before entry, he suffered an attack of pneumonia and had been chronically ill since. One month before entry, edema of the ankles appeared, and the dyspnea became severer. It was stated that he was partially digitalized elsewhere at this time. The evening before admission, the patient suddenly became much worse; he noted extreme dyspnea, with coughing, weakness and great malaise. He was referred to this hospital by a local physician.

Physical examination revealed an emaciated man propped up on the shock table and barely able to respond. He was dyspneic, cyanotic and acutely ill, so that the examination was necessarily cursory and brief. The chest was deformed. The respiratory excursions were small and asymmetric. The heart was enlarged, 10.5 cm to the left of the mid-sternal line at the fifth intercostal space. The right border of dullness was located 25 cm. to the right of the mid-sternal line. There was a loud blowing systolic murmur at the apex. The heart sounds were of fair quality. The radial and brachial arteries were moderately thickened, and there was a questionable slight engorgement of the neck veins. The abdomen was slightly distended, and a fluid wave was present. The dependent portions of the abdomen were dull to percussion. There was mild pitting edema of the ankles and sacrum. The scrotum was large.

The temperature was 100°F, the pulse 80, and the respirations 30.

Examination of the blood showed a red cell count of 4,800,000 with 90 per cent hemoglobin, and a white cell count of 28,000 with 82 per cent polymorphonuclears.

On admission, the patient was in extremis. He was dyspneic and semicomatose. He was given morphine sulfate, and a few minutes later the respirations fell to between 7 and 10 per minute. Coramine was given (2 cc intravenously), and the patient responded by talking and joking with his children.

X-ray examination of the chest at this time revealed the heart to be enlarged, without characteristic configuration. There was haziness in the right lower lung field, with questionably dilated bronchi in this area. Several minute areas of marked, increased density scattered through the right mid lung field had the appearance of old lipiodol. The patient was rushed to the ward, and slumped back into a nearly apneic state, with respirations again 7 to 10 per minute. He was placed in an oxygen tent, and given coramine subcutaneously every four hours, and digalen sub-

cutaneously every two hours for three doses. He lapsed into unconsciousness, and died about sixteen hours after admission.

### DIFFERENTIAL DIAGNOSIS

DR. F. DENNETTE ADAMS: The evidence provided by the history at the time of the first admission points toward chronic bronchopulmonary infection—tuberculous or nonspecific. The acute illness that ushered in the trouble may have been pneumonia—the duration of the attack, the severe cough and the bloody sputum are most suggestive. Nonspecific bronchopulmonary infection with bronchiectasis, I believe, can develop after pneumonia or certain other forms of acute respiratory disease. In the presence of this chronic ailment, recurrent episodes of acute bronchopulmonary infection are common, especially during the winter. Fever, cough and respiratory distress, often with the asthmatic form of breathing, characterize such attacks; between them, cough with purulent sputum, occasionally bloody sputum and, perhaps, wheezing respiration are the rule. Pulmonary tuberculosis, obviously, must also be considered, on the evidence provided by the history. Blood-streaked sputum, chronic cough and wheezing, especially if the last is unilateral, when they appear in middle life or beyond should always put one on the alert for bronchiogenic tumor. In this case, the duration of the illness is long for tumor.

The pain associated with coughing is best explained on the basis of a chronic pleuritis. The chronic indigestion seems to be of no importance so far as diagnosis is concerned.

The contraction of the upper half of the right chest and the crepitant rales at the right apex found on physical examination point toward chronic tuberculosis; so does the fact that the man had obviously lost weight. The musical rales, however, are more suggestive of chronic bronchitis or asthma. Nothing in the picture as a whole, however, points toward bronchial asthma as the underlying disturbance.

Failure to find tubercle bacilli in the sputum is of some significance, yet it by no means excludes active tuberculosis. It is rather surprising that the discharge diagnosis did not include at least a question of pulmonary tuberculosis, for there were low-grade fever, even with the patient in bed, bloody sputum, and clinical and roentgenologic evidence of disease at the apices.

With everything taken into consideration, I do not believe a definite diagnosis could have been established at the time of discharge from the first hospital admission.

Twelve years later, nineteen years after the trouble began, an acute episode starting less than a day earlier brought the patient back to the hospital. His symptoms of bronchopulmonary disease had continued, and he had also developed symptoms that were thought to have been related to his heart. More recently, increasing dyspnea and edema of the ankles had appeared.

On physical examination, dyspnea, cyanosis, enlargement of the heart, slight engorgement of the neck veins, ascites and dependent edema were noted—all indicative of right-sided heart failure. The patient also had slight elevation of temperature, definite elevation of respiratory rate and an elevated leukocyte count.

The roentgenologist reported cardiac enlargement and changes in the right lower-lung field. Nothing is stated about the changes previously noted in the upper-lung fields, but it is fair to assume that they were still present. Perhaps only additional changes, compared to those seen in the previous plate, were reported.

We have, then, a man first taken sick with a bronchopulmonary disturbance at the age of fifty, remaining chronically ill with respiratory-tract troubles for nineteen years, and eventually dying of what appears to be right-sided heart failure, with perhaps a terminal acute pulmonary infection. The last named is suggested by the fever and elevated leukocyte count. In my opinion, the problem can be reduced to that of deciding whether the underlying disturbance was tuberculous or nontuberculous. Despite the bloody sputum, the harassing cough and the wheezing, tumor can be excluded by the long course of the disease and the roentgenologic findings. A patient with a bronchiogenic tumor could hardly live this long and still have the diagnosis in doubt. The duration of the illness, the cough, bloody sputum and x-ray findings are consistent with tuberculosis. Yet they are just as consistent with nonspecific bronchopulmonary infection and bronchiectasis. Furthermore, the recurrent attacks of acute infection and the apparent development of right-sided heart failure are strong evidence in favor of the nontuberculous type of disease. It hardly seems likely to me that in the presence of active tuberculosis, the patient could have had so many acute episodes and still recover from them. With tuberculosis of sufficient severity to make him as sick as he was, one of the acute attacks might well have been even more serious or prolonged and resulted in earlier death, or at least after nineteen years one would expect a more characteristic clinical picture of chronic active tuberculosis. Furthermore, in tuberculosis of this duration, x-ray findings should be conclusive.

Taking all these factors into consideration, I am led to the conclusion that the patient died of chronic, nonspecific bronchopulmonary infection, bronchiectasis and cor pulmonale, with right ventricular failure. Acute bronchopneumonia was probably a terminal event. Healed tuberculosis of the apices is likely; the x-ray findings in the upper-lung fields cannot be disregarded.

A PHYSICIAN: Could this possibly be a cerebral embolus to explain the sudden death on this same basis?

DR. ADAMS: Cerebral embolus usually originates in the left auricle in cases of mitral stenosis with or without auricular fibrillation, in chronic auricular fibrillation from other causes, in the left ventricle in cases of coronary occlusion with left ventricular infarction, and in subacute bacterial endocarditis, involving the mitral or aortic valve. None of these were present in this case, nor were there any signs of a cerebral vascular accident.

A PHYSICIAN: Why do you rule out tuberculosis in your diagnosis?

DR. ADAMS: The course of the disease is not typical of tuberculosis, and at the end of nineteen years, changes in the lung more characteristic of progressive tuberculosis should be demonstrable roentgenologically.

#### CLINICAL DIAGNOSES

Bronchiectasis, with pneumonitis.  
Old pulmonary tuberculosis.  
Congestive heart failure.  
Cor pulmonale?

#### DR. ADAMS'S DIAGNOSES

Chronic nonspecific bronchopulmonary infection.  
Bronchiectasis.  
Cor pulmonale.  
Right ventricular failure.  
Terminal acute bronchopneumonia.  
Healed apical tuberculosis?

#### ANATOMICAL DIAGNOSES

Pulmonary emphysema.  
Pulmonary fibrosis, bilateral.  
Bronchiectasis.  
Bronchopneumonia, right lower lobe.  
Septicemia, *Staphylococcus aureus*.  
Cor pulmonale.  
Pulmonary tuberculosis, healed apical, bilateral.  
Arteriosclerosis, moderate cerebral, coronary and aortic.  
Peripheral edema.  
Pleuritis, chronic fibrous.  
Ascites.

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: The fundamental process in this case was a chronic, or perhaps more correctly recurrent, pulmonary infection and resultant destruction of the parenchyma of the lungs. At both apices were extensive scars that appeared quite characteristic of healed tuberculosis. There were no foci of activity. Elsewhere, there were extensive fibrosis and emphysema, as well as a diffuse bronchiectasis of many of the smaller radicles of the bronchial tree. It is very improbable that this was due to tuberculosis. There was a terminal acute infection, with spotted foci of early consolidation from which we grew *Staphylococcus aureus*.

The heart was moderately hypertrophied and markedly dilated on the right side, the right auricle being particularly capacious. The right ventricle measured 8 mm. in thickness, which is double the normal value. There can therefore be no doubt of the diagnosis of cor pulmonale. I assume that sudden right-sided heart failure, perhaps precipitated by an infection, was the explanation of the terminal episode. A little qualification is necessary, however, since the coronary arteries showed extensive atheroma, with marked narrowing of their lumens but no points of occlusion. There was enough coronary involvement, however, to make it possible that there was also some left-sided heart failure.

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THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

## AMERICAN ACADEMY OF PEDIATRICS

FROM October 8 to 11, the American Academy of Pediatrics will hold its eleventh annual meeting in Boston, with general headquarters at the Hotel Statler.

The membership of the academy, which is the largest pediatric society in the world, is made up of licentiates of the American Board of Pediatrics, and consists of 1400 pediatricians in the United States and Canada. The purpose of the organization—to elevate and maintain standards of practice, teaching, research and public health—is achieved through its annual and regional meetings and through its official organ, the *Journal of Pediatrics*. The academy, with the assistance of local committees and in collaboration with state

medical societies, supports federal, state and local agencies in child health, initiates such work in communities where the need exists, and prepares manuals containing information on immunization, vitamins and health records.

The American Academy of Pediatrics was one of the first medical groups to present subjects by the so-called "round-table method." This year, the program, as noted elsewhere in this issue of the *Journal*, will consist of round-table conferences on allergy, adolescence, feet and shoes, speech defects, orthodontia, adoption and other subjects. In addition to clinics at three Boston hospitals, there will be panel discussions by eminent authorities on vitamin B, intestinal obstruction, and growth and development. Surgeon General Thomas Parran and others will discuss the role of the pediatrician in national defense.

Owing to the large membership and limited seating facilities, the clinics and round-table conferences will be restricted to members of the academy; members of hospital staffs and public-health boards can be admitted without fee to the panel discussions and the scientific exhibits by presenting proper credentials at the registration desk, where guest badges may be obtained. Detailed information can be obtained from Dr. Lewis W. Hill, 319 Longwood Avenue, Boston, chairman of the Committee on Arrangements.

The Massachusetts Medical Society and the *Journal* extend a cordial welcome to the members of the American Academy of Pediatrics.

## THE SCHOOL LUNCH

THE Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association, taking cognizance of the importance of the school lunch, has recently released an official statement concerning this increasingly significant unit in the American dietary.

In adapting the school lunch to the needs of the child, one must recognize and correct the principal nutritional deficiencies most commonly found in American diets. These are calcium, vitamin

B<sub>1</sub> and, in certain areas, iron, iodine and the pellagra-preventive factors, nicotinic acid and riboflavin. Where money is actually lacking for the purchase of food, a deficiency in all the essentials may exist.

Further elaboration is found in the section concerning the food sources from which these deficiencies can be made up: milk for calcium, riboflavin and nicotinic acid; eggs for phosphorus and iron; cheese for calcium and phosphorus, vegetables, fruits and meats for many minerals, including iron; whole grains and the legumes for thiamin; and so forth. Practical elementary advice is given concerning the attractiveness of the diet, economic factors and care in preparation.

The proper and safe feeding of a vast multitude of people, whether in a congested city, in an army or in a nation, constitutes an appalling problem. Not only must a suitable diet be furnished,—and an increasing number of newly discovered factors must be considered,—but the difficulties of transportation and preservation and the economic laws of barter and exchange must be observed.

By and large, in this country, few persons need go hungry or badly nourished. A great deal of education in the selection and preparation of food is necessary, however. We have habituated ourselves to absorbing our calories on the move or at the counter without any loss of time, and with little regard to the balanced diet. A few years ago, at Harvard University, historic, impressive Memorial Hall was forced to close its kitchens and the infinite perspective of its great dining room the students, too impatient to sit, preferred to champ their hamburger rolls with one foot on a rail. If we do not mend our ways and find again the repose that comes from dining, even the Johnsonian\* era will come to an end, replaced by curb service—if the gasoline holds out!

\*H. ward

## MEDICAL EPONYM

### KARELL DIET

Philip J. Karell (1806-1886), physician to His Majesty, the Emperor of Russia, read a paper, "On the Milk Cure," before the Medical Society of

St Petersburg on March 8 and 23, 1865. This was first printed in the *St Petersburg medizinische Zeitschrift* (8: 193-220, 1865). A translation from the author's manuscript by Dr. G. L. Carrick appears in the *Edinburgh Medical Journal* (12, Pt. 1 97-122, 1866), and the essay in *Archives générales de médecine* (8: 513-533, 694-704, 1866). A portion of the translation follows:

After a great deal of experience, I have arrived at the conclusion, that in *all dropsies*, in *asthma*, when the result of emphysema and pulmonary catarrh, in obstinate *neuralgia*, when its cause lies in the intestinal canal, in diseases of the *liver* (simple hypertrophy and fatty degeneration), and generally in diseases where there is faulty nutrition milk is the best and surest of remedies.

I generally commence the cure by employing milk *alone*, and forbidding all *other kinds of nourishment*. I proceed with great caution in prescribing for the patient, three or four times daily, and at *regularly observed intervals*, half a tumbler or a tumbler, *i.e.*, from 2 to 6 ounces, of skimmed milk. During the second week two ordinary quarts are generally administered each day.

R. W. B.

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

#### ALBUMINURIA, FOLLOWED BY FATAL SEPSIS

A thirty-one year-old primipara was sent into the hospital about three weeks before the expected date of confinement because of albuminuria and a systolic blood pressure of 160.

The care during pregnancy had not been entirely satisfactory. The patient had been seen in the third month but probably not again until the seventh month, when nothing abnormal was noted. In the thirty-sixth week, the blood pressure had risen to 150 systolic, 100 diastolic, and a large trace of albumin had appeared in the urine; a good deal of edema was also present. The next week, the blood pressure was 160 systolic, and the patient was sent into the hospital for induction.

Induction of labor was considered because of the albuminuria and hypertension. Labor was induced by the rupture of the membranes, and after ten hours, twins were delivered. The first baby was delivered by low forceps, and the second by version. Three days after delivery, the temperature rose, at the same time, the patient developed a sore throat. She developed phlebitis, a septic

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, Secretary, 330 Dartmouth Street, Boston.

hip, abscess in the back, many pulmonary infarcts and osteomyelitis of the hip. She was transfused twice. Prontylin was given, but not until the one hundred and twenty-first day of hospitalization. The patient died one hundred and forty-four days after delivery, the temperature vacillating all the time from the third day. Permission for an autopsy was not obtained.

*Comment.* This case represents a type of sepsis that was not infrequently seen years ago. There was no report of blood culture, but such cases are frequently staphylococcal in origin. It is perfectly possible that the infection was induced by the sore throat. It is more probable that the rupture of the membranes and the uterine manipulations of forceps and version were contributory causes. Chemotherapy, applied as it would be today, very early in the onset of this condition might have changed the course of the disease. If the infection had been caused by a streptococcus, it is almost certain that the fatal outcome would have been prevented; if it had been staphylococcal, it is possible that immune transfusions, resorted to early, would have changed the result. Today, any patient who shows signs of infection after delivery should have cultures taken from the throat, blood stream and uterus to determine the specific etiology. After the organism has been identified, intelligent therapy should be instituted immediately. The uterus itself should never be entered. Chemotherapy should be applied in cases in which the organism is one for which the treatment by chemotherapy is known to be valuable. When the infection is staphylococcal, immune transfusions—even though they entail much skilled laboratory work—should be attempted unhesitatingly. All such cases in open wards should be isolated for the protection of other patients. If isolation in puerperal sepsis is not scrupulously followed, epidemics may quickly result. There are about eighty-five deaths each year from puerperal sepsis in Massachusetts. The number should be markedly reduced by the intelligent use of chemotherapy and the intelligent handling of all cases by isolation in maternity hospitals. It must be remembered that even though chemotherapy is invaluable, prevention is more valuable, and that until more adequate supervision is made possible throughout the State,—thereby ensuring clean, gentle operative obstetrics when it is necessary and eliminating much operative obstetrics that would thus be proved unnecessary,—the number of deaths from sepsis will not be materially reduced.

## STATED MEETING OF THE COUNCIL

A stated meeting of the Council will be held in John Ware Hall, Boston Medical Library, 8 Fenway, Boston, on Wednesday, October 1, 1941, at 10:30 o'clock.

### *Business:*

1. Presentation of record of meeting held May 21 and 22, 1941, as published in the *New England Journal of Medicine* for June 26, 1941.
2. Reports of standing and special committees.
3. Appointment of an auditing committee.
4. Fill any vacancies in the offices of the Society.
5. Such other business as may lawfully come before this meeting.

MICHAEL A. TIGHE, *Secretary.*

### IMPORTANT ADDENDA TO BE CONSIDERED BY THE COUNCIL

The Executive Committee will submit the following resolution. The necessity for this resolution has grown out of the confusion which has arisen in the interpretation of certain phraseology contained in Chapter V, Section 2 of the By-Laws of the Massachusetts Medical Society. The resolution, which seeks to have the Council of the Massachusetts Medical Society interpret this language, is as follows:

*Whereas*, the Massachusetts Medical Society is desirous that all skillful and ethical practitioners of medicine in Massachusetts shall be members of the Massachusetts Medical Society;

*Whereas*, Chapter V, Section 2, of the By-Laws of the Massachusetts Medical Society provides the means by which practitioners in medicine in Massachusetts may become members of the Massachusetts Medical Society;

*Whereas*, by the language involved in Chapter V, Section 2, of the By-Laws of the Massachusetts Medical Society the Council of the Massachusetts Medical Society intends that it shall have accurate knowledge of the training, medical skill and ethical conduct of those who seek admission to membership in the Massachusetts Medical Society;

*Whereas*, in the case of graduates of nonapproved schools, Chapter V, Section 2, of the By-Laws of the Massachusetts Medical Society provides that the applicant for membership in the Massachusetts Medical Society shall have been in the practice of medicine for a minimum of five years;

*Whereas*, in establishing such a period of probation for graduates of nonapproved schools, the Council of the Massachusetts Medical Society intends that it shall have had opportunity to closely observe the medical skill and ethical conduct of such applicants;

*Whereas*, in the case of most graduates of foreign medical schools who have been in the practice of medicine for five years in foreign countries, the Council of the Massachusetts Medical Society has no opportunity to know of the training or adequately observe the medical skill and ethical conduct of such medical practitioners; therefore be it

*Resolved*, that the Council of the Massachusetts Medical Society interprets the phrase who has practiced for a minimum of five years, as appearing in the By Laws of the Massachusetts Medical Society, Chapter V, Section (b), to mean what is meant by the phrase, who has fully practiced medicine for a minimum of five years in the United States, be it further

*Resolved*, that the Council of the Massachusetts Medical Society shall be considered to have accurate knowledge of the medical training and medical skill of such graduates foreign medical schools who have practiced medicine in foreign countries for five years and who are eminent in the profession of medicine and well known to the Council of the Massachusetts Medical Society for their scientific attainments, provided such practitioners shall have satisfied the Council of the Massachusetts Medical Society that their medical practice has been ethical according to the standards as set down in the Code of Ethics of the American Medical Association

The Executive Committee will recommend to the Council of the Massachusetts Medical Society that at the annual meeting of the Council of the Massachusetts Medical Society take place on the evening before the annual meeting of the Society, and that the annual meeting of the Society be moved up from the second day of the annual meeting to the first day

It is believed that this does not involve any changes in the By Laws

If this recommendation is adopted, members of the Council will have an opportunity to attend the scientific exercises throughout these sessions. This opportunity has been seriously curtailed under the present setup

The following is submitted by the Special Committee Concerned With Prepayment Medical Care Costs Insurance. This matter comes to the Council as a part of the report of and with approval of the Committee on Public Relations, the Executive Committee has considered this presentation of great length and recommends it to the earnest consideration of the Council. It has to do with tentative set of by laws to govern a corporation (The Massachusetts Medical Service) proposed to be set up under the permissive legislation passed by the current session of the Massachusetts Legislature

## ARTICLE I

### PRINCIPAL OFFICE AND SEAL

*Section 1* The principal business office of the corporation shall be in the City of Boston, County of Suffolk, Commonwealth of Massachusetts.

*Section 2* The seal shall be circular in form with the words Massachusetts Medical Service around the periphery and the words and figures 1941 Massachusetts within

## ARTICLE II

### MEMBERSHIP OF THE CORPORATION

*Section 1* The members of the corporation shall consist of those persons who shall from time to time be the

members of the Executive Committee of the Massachusetts Medical Society

*Section 2* Each member of the corporation shall be entitled to one vote

*Section 3* The annual meeting of the members of the corporation for the choice of directors and the transaction of such other business as shall properly come before the meeting shall be held at the office of the corporation in the City of Boston, or at such other place as may be stated in the call of the meeting, on the last Tuesday of March in each year if not a legal holiday and if a legal holiday then on the next secular day following. In case the annual meeting shall not be duly called and held, the Board of Directors shall call a special meeting in lieu of and for the purpose of such annual meeting and all proceedings at such special meeting shall have the same force and effect as at an annual meeting

*Section 4* Special meetings of the members shall be called by the clerk whenever the Board of Directors or the President shall so order, or upon written request of three or more members, and such request shall state the purpose of such meeting

*Section 5* Notice of the annual meeting and of all special meetings of the members shall be given by the clerk by mailing or delivering to each member at least seven days before the day fixed for the meeting a notice stating the place, day and hour and purpose of the meeting

*Section 6* At every meeting of the members, there shall be represented in person or by proxy at least a majority of the members to constitute a quorum, but a smaller number may adjourn from time to time.

## ARTICLE III

### BOARD OF DIRECTORS

*Section 1* The affairs, property and business of the corporation shall be managed by a board of fifteen directors who may exercise all such powers of the corporation as are not by law or by these by laws required to be otherwise exercised. Directors need not be members of the corporation

A majority of the directors shall at all times be persons approved in writing by the Massachusetts Medical Society. One third of the directors shall be physicians registered to practice medicine in the Commonwealth of Massachusetts and engaged in the active practice of medicine in the Commonwealth, and one third shall be persons who are or who agree to become subscribers to the nonprofit medical service plan to be operated by the corporation

*Section 2* The incorporators at their first meeting shall elect five directors to hold office until the first annual meeting, five to hold office until the second annual meeting, and five to hold office until the third annual meeting. At each annual meeting, the members of the corporation shall elect five directors to hold office for a term of three years and thereafter until their successors are elected, provided, however, that at least thirty days before each annual meeting the members shall submit to the President of the Massachusetts Medical Society a list of those persons whom they propose to elect as directors

*Section 3* Any director may be removed from office by a majority of the members of the corporation either by writing filed with the clerk of the corporation or by a vote passed at a meeting of the said members

*Section 4* Vacancies in the Board of Directors occurring during the year shall be filled by a majority vote of those members present at a meeting duly called for such

purpose, provided, however, that at least thirty days prior thereto the members shall submit to the President of the Massachusetts Medical Society the name of the person they propose to elect as a director.

*Section 5.* A majority of the directors in office for the time being shall constitute a quorum for the transaction of business, but a smaller number may adjourn from time to time.

*Section 6.* Regular meetings of the directors shall be held immediately after the adjournment of the annual meeting of the members of the corporation at the place of holding the annual meeting and at such times and places as the Board of Directors may determine and no notice of such meetings shall be necessary. Special meetings may be held in like manner and shall be called by the clerk whenever the President or any three directors shall so request in writing, and three days' notice of such meetings shall be given to each director not joining in the request for such meetings unless shorter notice shall be reasonable in the circumstances. Any meeting of the Board of Directors shall be a legal meeting without notice if each director, by a writing filed with the record of the meeting, waives such notice.

*Section 7.* The Board of Directors shall have power to purchase any property or rights and to enter into any contracts which they deem advantageous to the corporation, to fix the price to be paid by the corporation for such property, rights or contracts, to borrow money, to issue bonds, debentures or other securities of the corporation and pledge or sell the same for such sums and at such prices as they may deem expedient, to adopt rules and regulations subject to the provisions of Article IV hereof and in general to exercise such other powers and to do all such other things as are not required by any other article of the by-laws to be exercised or done by any committee named therein.

No contract or other transaction between this corporation and any other corporation shall in any way be affected or invalidated by the fact that any of the directors of this corporation are pecuniarily or otherwise interested in or are directors of such other corporations and any director of this corporation may be a party to and may be pecuniarily or otherwise interested in any contract or transaction of this corporation provided that the fact that he is so interested shall be disclosed or shall be known to the Board of Directors or a majority thereof and his vote shall not be necessary to authorize or ratify any such contract or transaction.

*Section 8.* Directors as such shall not receive any stated salary for their services, but by resolution of the board a fixed sum and expenses of attendance, if any, may be allowed for attendance at board meetings. Nothing herein contained shall be construed to preclude a director from serving the corporation in any other capacity and receiving remuneration for such service.

*Section 9.* The Board of Directors may from time to time delegate any of its powers to committees or officers, attorneys or agents of the corporation subject to such regulations as may be adopted by the board.

## ARTICLE IV

### COMMITTEES

*Section 1.* The directors may appoint such committees as they deem necessary, including an Administrative Committee and a Finance Committee, and they shall appoint a Central Professional Committee and an Actuarial Research Committee as provided herein.

*Section 2.* There shall be a Central Professional Service Committee composed of five directors appointed by the president of the corporation, of whom four including the chairman shall be physicians registered to practice in the Commonwealth of Massachusetts. The chairman of the Committee shall be designated by the president of the corporation.

*Section 3.* The Central Professional Service Committee shall have delegated to it control and supervision of the medical aspects of all matters relating to (a) the standards of medical care to be furnished subscribers, (b) the qualifications of specialists, (c) the extent and classification of medical benefits to be furnished subscribers, (d) the determination of income groups eligible to become subscribers, (e) the compensation to be paid participating physicians, and (f) the admission, suspension and discipline of participating physicians. All rules and regulations of the corporation relating to the foregoing shall be initiated by the Central Professional Service Committee, provided, however, that any rule or regulation relating to the determination of income groups eligible to become subscribers shall first be approved by the Council of the Massachusetts Medical Society. Whenever the committee shall initiate any change in a rule or regulation, it shall give at least thirty days' notice thereof to the President of the Massachusetts Medical Society.

*Section 4.* In the event of a complaint relative to the conduct or services of a participating physician or of any controversy between a participating physician and a subscriber or whenever it has reason to believe that a participating physician has been guilty of a violation of the rules and regulations of the corporation, or unprofessional or unethical conduct or of conduct which is liable to endanger the interests of the corporation or of any of its subscribers, the committee shall refer the matter for investigation to the District Professional Service Committee within whose district the physician concerned has his principal office, which shall investigate the matter and shall then report the result of its investigation to the Central Professional Service Committee. If it appears to the Central Professional Service Committee that there is reasonable cause to believe that the participating physician has been guilty of a violation of the rules and regulations of the corporation, of unprofessional or unethical conduct, or of conduct which is liable to endanger the interests of the corporation or of any of its subscribers, it shall assign a date for a hearing giving the participating physician concerned at least seven days' notice thereof. If at the hearing, at which the participating physician shall be given full opportunity to be heard, the said committee shall find the said physician guilty, it shall terminate the agreement between the said physician and the corporation, or it may take any other disciplinary action which is proper and appropriate in the circumstances, having first, however, reported to the President of the Massachusetts Medical Society its findings and having obtained his approval of its proposed action.

*Section 5.* The Central Professional Service Committee shall report its acts and proceedings to the Board of Directors at such times as the Board of Directors shall require.

*Section 6.* There shall be an Actuarial Research Committee of at least three directors appointed by the president of the corporation who shall designate one of the members as chairman.

*Section 7.* The Actuarial Research Committee shall obtain actuarial data as to incidence of demand for medical services and the cost thereof, shall analyze the data and



and report to the Board of Directors hereon. It shall have the power, subject to the approval of the Board of Directors, to engage such persons to assist in this work as it may deem necessary.

## ARTICLE V

### OFFICERS

*Section 1* The officers of the corporation shall be a president, a treasurer, a clerk and such subordinate officers as the Board of Directors shall from time to time appoint with such powers and duties and for such terms of office as the directors may designate. The president shall be chosen from among the directors of the corporation; no other officers need not be. The directors at their annual meeting in each year shall elect the aforesaid officers, provided, however, that the incorporators at their first meeting shall elect a treasurer and clerk to hold office until the first annual meeting. All of the said officers shall hold their respective offices for one year and thereafter until their successors are elected and qualified, subject, however, to removal at any time by vote of a majority of the Board of Directors, except that the officers appointed at the first meeting of the Board of Directors shall hold office only until the first annual meeting and thereafter until their successors are elected and qualified. Vacancies in any of the said offices shall be filled for the unexpired portion of the term by the Board of Directors. Officers may be paid such salary or compensation as the Board of Directors shall determine.

*Section 2* The president shall be the chief executive officer of the corporation. He shall preside at all meetings of the Board of Directors. He shall see that all orders and resolutions of the Board of Directors are complied with.

*Section 3* The treasurer shall have charge of the corporation's financial affairs, subject however to the supervision and control of the Board of Directors. He shall have the custody of all money and securities except his own bond, which shall be kept by the president. He shall deposit all money and valuables in the name and to the credit of the corporation in such depositories as shall be determined by the Board of Directors. He shall disburse the funds of the corporation as ordered by the Board of Directors. He shall keep or cause to be kept the corporation's accounts in suitable books wherein every transaction shall be accurately recorded and shall render to the president and directors at regular meetings of the board whenever they require it an account of his transactions as treasurer and of the financial condition of the company and shall discharge all other duties properly appertaining to his office or which may be attached thereto by the Board of Directors. He shall give bond for the faithful discharge of his duties in such form and in such sum as the Board of Directors may require.

*Section 4* The clerk shall keep the records of all meetings of the members and of the Board of Directors and shall give notice of all meetings required by these bylaws. He shall have the custody of the record books of the corporation and shall perform all duties usually incident to the office of clerk and such other duties as may be from time to time assigned to him by the Board of Directors.

## ARTICLE VI

### DISTRICT COMMITTEES

*Section 1* Each district medical society in the Commonwealth may appoint a District Administrative Unit composed of not more than nine members of whom a

majority shall be physicians engaged in active practice within the district and shall designate one of the members of the committee who is a physician as chairman.

*Section 2* Each District Administrative Unit shall assist in the operation of the medical service plan and in obtaining subscribers thereto within its district and shall perform such duties as the Board of Directors may prescribe. It shall from time to time make recommendations to the Board of Directors as to any phase of the operation of the medical service plan except one within the jurisdiction of the District Professional Service Committee.

*Section 3* Each district medical society may appoint a District Professional Service Committee, composed of at least five physicians engaged in active practice within the district and shall designate one member thereof as chairman.

*Section 4* Each District Professional Service Committee shall act in co-operation with and under the supervision of the Central Professional Service Committee. It shall from time to time survey the quality of medical care rendered to subscribers within its district and shall report thereon to the Central Professional Service Committee. It may report to the Central Professional Service Committee on the qualifications of specialists within its district and may compile and from time to time revise, under the supervision of the Central Professional Service Committee, a list of specialists within its district according to the accepted policy of the Massachusetts Medical Society, which may be used for the benefit of subscribers to the medical service plan. It shall make recommendations to the Central Professional Service Committee as to all matters within its jurisdiction.

*Section 5* Each District Professional Service Committee shall, whenever any matter relating to the services or conduct of a participating physician or relating to a controversy between a participating physician and a subscriber is called to its attention by complaint or otherwise, fully investigate the matter and report hereon to the Central Professional Service Committee.

## ARTICLE VII

### SUBSCRIBERS

*Section 1* A resident of the Commonwealth may become an unlimited subscriber to the medical service plan provided that his annual income does not exceed such amount as shall be fixed by the Board of Directors as provided in Article III, Section 7, and provided further that he make application to become a subscriber as one of such a group as the Board of Directors may specify.

*Section 2* An unlimited subscriber shall be entitled to receive from a participating physician such medical services as are included in the subscriber's contract with the corporation, subject to whatever rules and regulations may be adopted by the Board of Directors relative thereto.

*Section 3* A resident of the Commonwealth may become a limited subscriber to the medical service plan if his annual income exceeds such amount as shall be fixed by the Board of Directors on such terms and conditions as the Board of Directors may by regulations prescribe.

*Section 4* A limited subscriber shall be entitled only to such benefits as are provided in his contract with the corporation. The corporation shall have no supervision over the amount to be charged by a participating physician for services to a limited subscriber.

*Section 5* Subscribers shall have free choice among participating physicians subject to the provisions of Article

VIII, Section 3 hereof, and to the rules and regulations adopted by the Board of Directors.

*Section 6.* The Board of Directors shall have power to enter into arrangements and agreements with employers, societies, charitable organizations, and governmental agencies and authorities for the payment of part or all of the cost of medical care furnished to any persons who may be entitled to such care under the rules and regulations adopted by the Board of Directors.

## ARTICLE VIII

### PARTICIPATING PHYSICIANS

*Section 1.* Any physician registered to practice in the Commonwealth may become a participating physician on complying with the provisions of these by-laws and the rules and regulations of the corporation.

*Section 2.* A physician desiring to become a participating physician shall make written application in the form prescribed by the rules and regulations and shall before becoming entitled to act as a participating physician enter into a written agreement with the corporation in the form prescribed by the rules and regulations.

*Section 3.* A participating physician shall have the right to accept or reject patients so far as subscribers are concerned and the right to discontinue treatment of any subscriber according to the code of ethics of the American Medical Association, provided, however, he shall not have the right to refuse to accept a subscriber as a patient or to continue treatment of a subscriber for the sole reason that he is a subscriber and such refusal shall constitute grounds for the termination by the corporation of its agreement with a participating physician.

*Section 4.* A participating physician shall not request or accept from anyone whom he knows to be an unlimited subscriber any compensation for such services as such subscriber is entitled to under his contract with the corporation, except such initial service charge, if any, as may be required by the rules and regulations adopted by the Board of Directors.

## ARTICLE IX

### AMENDMENT OF BY-LAWS

*Section 1.* These by-laws may be amended or repealed by vote of the majority of the members of the corporation.

## MISCELLANY

### RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JULY, 1941

DISEASES	JULY 1941	JULY 1940	FIVE YEAR AVERAGE*
Anterior poliomyelitis	5	3	9
Chicken pox	519	384	380
Diphtheria	9	7	18
Dog bite	1336	1353	1211
Dysentery, bacillary	26	97	25
German measles	116	30	53
Gonorrhea	344	335	426
Lobar pneumonia	155	183	175
Measles	1420	2830	1331
Meningitis, meningococcal	5	0	3
Meningitis, other forms	8	—	—
Mumps	534	358	313
Paratyphoid fever	4	12	10
Scarlet fever	232	196	240
Syphilis	388	424	442
Tuberculosis, pulmonary	224	255	306
Tuberculosis, other forms	31	18	30
Typhoid fever	5	3	15
Undulant fever	4	4	4
Whooping cough	659	521	520

\*Based on figures for preceding five years

### GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from: New Bedford, 3; Quincy, 2; total, 5.

Diphtheria was reported from: Arlington, 1; Boston, 2; Fall River, 3; Gloucester, 1; Somerville, 1; Taunton, 1; total, 9.

Dysentery, bacillary, was reported from: Arlington, 2; Boston, 1; Salem, 1; Waltham, 9; Worcester, 12; Wrentham, 1; total, 26.

Infectious encephalitis was reported from: Waltham, 1, total, 1.

Meningitis, meningococcal, was reported from: Boston, 1; Camp Edwards, 1; Everett, 1; Milford, 1; Palmer, 1; total, 5.

Meningitis, other forms, was reported from: Arlington, 1; Chicopee, 1; Haverhill, 1; Lawrence, 1; Palmer, 1; Quincy, 1; Springfield, 1; Worcester, 1; total, 8.

Paratyphoid fever was reported from: Beverly, 1; Boston, 1; Haverhill, 1; Saugus, 1; total, 4.

Pellagra was reported from: Boston, 1; Wakefield, 1; total, 2.

Septic sore throat was reported from: Arlington, 1; Boston, 3; Brockton, 1; Easton, 1; Somerville, 1; Waltham, 1; total, 8.

Tetanus was reported from: Quincy, 1; total, 1.

Trachoma was reported from: Boston, 1; New Bedford, 1; total, 2.

Typhoid fever was reported from: Boston, 1; Brockton, 1; Dennis, 1; Haverhill, 1; Middleboro, 1; total, 5.

Undulant fever was reported from: Leominster, 1; Westboro, 1; West Brookfield, 1; Whitman, 1; total, 4.

Chicken pox, German measles, mumps and whooping cough showed the usual seasonal decline but were reported above the five-year averages.

Meningitis, both meningococcal and other forms, continued above normal levels.

Dog bite, bacillary dysentery, measles, scarlet fever and undulant fever were at about the expected prevalence for the season.

Anterior poliomyelitis, diphtheria, gonorrhea, lobar pneumonia, paratyphoid fever, syphilis, pulmonary tuberculosis and typhoid fever were less prevalent than usual.

## BOOK REVIEWS

*Chest X-Ray Interpretation, with Special Reference to Tuberculosis.* By J. Burns Amberson, Jr., M.D. 8<sup>th</sup>, 2<sup>nd</sup> ed., 48 pp., with 30 illustrations. New York: National Tuberculosis Association, 1941. 25 cents.

This small brochure is a short discussion and a description of the commoner x-ray findings in pulmonary tuberculosis. The author has had many years of experience in both diagnosis and treatment of pulmonary tuberculosis. In addition, because of his many years as a student of tuberculosis, he is well qualified for this work.

The book includes an excellent discussion of the technical aspects of x-ray examinations, as well as an intelligent and judicious consideration of the pathogenesis and evolution of tuberculosis, indications for x-ray examinations of the chest, and roentgenographic appearances and interpretations of tuberculous lesions. With the greater popularity of the x-ray apparatus as the standard part of the internist's and the general practitioner's office equipment, intelligent guidance in this subject is indeed welcome. The busy practitioner will find a good deal of common sense as well as sound scientific material clearly written.

and well illustrated Dr William C Cutter in his foreword cautions, however, against too much self reliance by the internists and points out the necessity of expert radiologic consultation, which is still a factor of the medical service.

The National Tuberculosis Association has previously published many authoritative small volumes on different phases of tuberculosis. This brochure is an excellent addition to this fine series of publications and should be read by all interested in the subject of pulmonary tuberculosis.

*Emergency Surgery* By Hamilton Bailey, FRCS Fourth edition 8°, cloth, 944 pp., with 930 illustrations. Baltimore: Williams and Wilkins Company, 1940 \$10.00

In reading this book, one is struck by the diversity of material presented, for it includes all phases of emergency surgery in various parts of the body. It is to be remembered that in England specialization is far behind the practice of metropolitan America. Over there, a general surgeon is such in fact and can be summoned to deal with any surgical condition by a fellow practitioner. This book represents the wealth of experience accumulated by the more successful surgeon under such a system.

This is the sort of meaty volume that a general surgeon in the smaller hospital enjoys. It solves many of his practical problems, while introducing a minimum of the theory that only confuses a busy practitioner. But this feature also adds an element of weakness, in that some well-established procedures of recent origin are not considered in detail. The Miller-Abbott tube is described but its use is not specifically recommended in the treatment of the paralytic ileus that so often accompanies peritonitis. Cecostomy and ileostomy, however, are recommended as useful measures in this condition. In discussing the administration of parenteral fluids over a period of days, the author notes the threat of edema but he does not counsel the use of distilled water and glucose in proper amounts to offset the positive balance of sodium chloride.

One of the outstanding features of the editorial policy used by the author is the case history. This has been largely abandoned in modern textbooks in which the statistical method is presented. However, the case history defines the specific problem far better than a group of figures, and in this book it is used with good effect.

This volume and the book on war surgery edited by the same author are two works that will be appreciated by all who deal with surgical emergencies.

*Age Morphology of Primary Tubercles* By Henry C Sweeney, MD 8°, cloth, 265 pp., with 73 illustrations. Springfield, Illinois: Charles C Thomas, 1941 \$5.00

This book describes an interesting and extensive clinicopathological investigation of the primary type of tuberculous infection in man. In his studies, the author found a rather remarkable similarity of structure in tubercles of the same approximate age. He also found a definite sequence of changes in all tubercles with respect to maturation, degeneration, regeneration and metaplasia.

In this interesting and novel study, both from pathologic specimens and from thorough x-ray examinations, he concludes that about 90 per cent of the primary infections in which the calcified residues persist may be given an age rating by pathological methods that are accurate within plus or minus 25 per cent in lesions between six months

and twenty years of age. The age determination of the tubercle by pathological methods was followed on many contacts and on many selected cases to determine the potential relation of tuberculosis to attacks of pleurisy and pneumonia and to occupations, such as the nursing of tuberculous patients. In most studies, the results were, according to the author, surprisingly accurate. In life, however, this study was found to have little importance, because he found that only about 20 per cent of such primary tuberculous infections are visualized on the x-ray film. He also noted what most of us were taught previously: any lesion that is large and not well calcified is potentially dangerous. In addition, the soft lesions are dangerous.

In a series of cases that were kept under control, such as those of nurses and hospital attendants, the author traced the tuberculous infection to the period of contact at the hospital or sanatorium and obtained certain constant morphologic changes. Thus, he believes that in such cases the method might be applied in determining the liability as well as the probable source of the infection. In addition, he employed this method with some success in studying the reinfectious type, especially when repeated tuberculous infection had been spaced over a period of years. The book offers very interesting and intriguing material for the pathologist and should stimulate as well as help the research worker in the field of tuberculosis. However, the facts that ante-mortem x-ray films reveal only 20 per cent of primary lesions, of which only part reveal any age changes, and that most of them demonstrate no changes after eight years are rather discouraging to the clinicians.

The volume should make a very valuable addition to the library of men engaged in tuberculosis work.

*Help Your Doctor to Help You When You Have Sick Headache or Migraine* Edited by Walter C Alvarez editor in chief, George Blumer, Logan Clendening, Irving Cutter, Howard W Haggard, Rudolph Matas, Charles W Mayo, George R Minot, John H Stokes and George H Whipple 8°, cloth, 37 pp. New York: Harper and Brothers, 1941 95 cents

An editorial board of ten distinguished physicians is sponsoring a series of booklets, each dealing with a common complaint. The authorship of these booklets is anonymous, but internal evidence points to the gastroenterology department of the Mayo Clinic as the probable birthplace of the booklet on migraine. Obviously, the writer is an authority on the subject and presents his points of view clearly and forcefully. The only criticism of the medical treatment of the subject is the almost exclusive emphasis on psychic (emotional) factors, and warnings against mistreatment of the brain, whatever that means.

Efforts to educate patients to co-operate intelligently with their physicians are laudable. The task of supplementing without supplanting the individualized advice of the patient's physician is not easy, and in this respect the author of the booklet speaks like a professor of medicine, directly advising the patient, and not like a self-effacing, diplomatic assistant to the patient's physician. He disparages the efforts of the physician by repeated examinations to discover contributing causes of the headaches and to correct physical abnormalities, which have no proved influence in all cases of migraine. Apparently, the patient puts himself on an elimination diet and selects a headache reliever. Only once was the reviewer able to

## UNITED STATES NAVAL HOSPITAL

The dates, subjects, and speakers for the 1941-1942 medical meetings at the United States Naval Hospital in Chelsea are listed below. The meetings are scheduled to begin at 8:15 p.m., and are open to those who are interested.

October 10—The Nature and Treatment of Organic Arterial Disease. Dr. Edward Edwards.

November 14—The Modern Treatment of Pneumonia. Dr. Maxwell Finland.

December 1—The Management of Hand Injuries and Infections. Dr. Henry Marble.

January 9—Blood Transfusions. Dr. Francis T. Hunter.

February 13—Head Injuries. Dr. Donald Munro.

March 13—Evaluation of Surgical Risk from a Cardiovascular Viewpoint. Dr. Samuel A. Levine.

April 10—The Relation between Renal Infection and Hypertension. Dr. Soma Weiss.

SEVENTH POSTGRADUATE SEMINAR  
IN NEUROPSYCHIATRY

The Metropolitan State Hospital, Waltham, recently announced the opening of the Seventh Postgraduate Seminar in Neuropsychiatry.

The course consists of three units: military neuropsychiatry, October 3 to 31; general psychiatry, November 3 to December 12; and general neurology, January 5 to April 10. It is open to a limited number of graduate physicians. The teaching staff comprises a number of recognized specialists in this field throughout the state, and is under the direction of Dr. Roy D. Halloran, superintendent, Metropolitan State Hospital, and Dr. Paul I. Yakovlev, clinical director, Walter E. Fernald State School.

## SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING  
SUNDAY, SEPTEMBER 21

TUESDAY, SEPTEMBER 23

8 p.m. Massachusetts Society of X-Ray Technicians. Massachusetts Memorial Hospitals.

WEDNESDAY, SEPTEMBER 24

\*12 m. Clinicopathological conference. Children's Hospital.

\*Open to the medical profession.

SEPTEMBER 23—MAY 26. Massachusetts Society of X-Ray Technicians, Inc. Page xii, issue of September 11.

OCTOBER 8-11. American Academy of Pediatrics, Boston. Page 473.

OCTOBER 9-MAY 14. Pentucket Association of Physicians. Page 473.

OCTOBER 10-APRIL 10. United States Naval Hospital, Chelsea. Notice above.

OCTOBER 13-24. 1941 Graduate Fortnight of the New York Academy of Medicine. Page 834, issue of May 8.

OCTOBER 14-17. American Public Health Association. Page 579, issue of March 27.

OCTOBER 19-23. American Academy of Ophthalmology and Otolaryngology. Page 350, issue of August 28.

OCTOBER 29-30. New England Postgraduate Assembly. Pages ii-iii, issue of September 11.

OCTOBER 29-NOVEMBER 1. Association of Military Surgeons. Page 473.

NOVEMBER 3-7. American College of Surgeons. Page vii, issue of July 31.

NOVEMBER 5-6. American Conference on Industrial Health. Page 473.

JANUARY 3. American Board of Obstetrics and Gynecology. Page 473.

JANUARY 10-11. Forum on Allergy. Page 392, issue of September 4.

APRIL 20-24. American College of Physicians. Page 996, issue of June 5.

## DISTRICT MEDICAL SOCIETIES

## BERKSHIRE

OCTOBER 30.

APRIL 30.

## BRISTOL NORTH

SEPTEMBER 18. North Attleboro.

APRIL 16. Taunton.

## ESSEX NORTH

SEPTEMBER 24. Governor Dummer Academy, South Byfield.

JANUARY 7. Haverhill.

MAY 6. Lawrence.

## ESSEX SOUTH

SEPTEMBER 24. Governor Dummer Academy, South Byfield (joint meeting with Essex North District).

NOVEMBER 12. Beverly Hospital, Beverly.

DECEMBER 3. Salem Hospital, Salem.

JANUARY 7. Danvers State Hospital, Hathorne.

FEBRUARY 11. Lynn Hospital, Lynn.

MARCH 4. Essex Sanatorium, Middleton.

APRIL 1. Addison Gilbert Hospital, Gloucester.

MAY 13. Annual meeting (place to be announced).

## FRANKLIN

NOVEMBER 11.

JANUARY 13.

MARCH 10.

MAY 12. Annual meeting.

Meetings will be held at the Franklin County Hospital at 11.00 a.m.

## HAMPSHIRE

NOVEMBER 5. Veterans Hospital, Leeds, 4:30 and 6:00 p.m.

JANUARY 7. Belchertown State Hospital, 1:00 and 4:00 p.m.

MARCH 4. Hotel Northampton, Northampton, 4:30 and 6:30 p.m.

MAY 6. Hotel Northampton, Northampton, 8:30 p.m.

## MIDDLESEX EAST

NOVEMBER 12.

JANUARY 28.

MARCH 18.

MAY 6.

All meetings will be held at 12:15 p.m. at the Bear Hill Golf Club, Stoneham, except that of May 6, which will be held at Woburn at 6:30 p.m.

## MIDDLESEX NORTH

OCTOBER 29.

JANUARY 28.

APRIL 29.

## NORFOLK SOUTH

OCTOBER 2.

NOVEMBER 6.

DECEMBER 4.

JANUARY 8.

FEBRUARY 5.

MARCH 5.

APRIL 2.

MAY 7.

All meetings will be held at 12:00 noon at the Norfolk County Hospital, South Braintree, with the exception of that of February 5, which will be held at the Quincy City Hospital, Quincy.

## PLYMOUTH

OCTOBER 16. Moore Hospital, Brockton.

NOVEMBER 20. Plymouth County Hospital, South Hanson.

JANUARY 15. Brockton Hospital, Brockton.

FEBRUARY 19. Jordan Hospital, Plymouth.

MARCH 19. Goddard Hospital, Brockton.

APRIL 16. Bridgewater State Farm, Bridgewater.

MAY 21. Lakeville Sanatorium, Middleboro.

## WORCESTER

OCTOBER 8. Rutland State Hospital, Rutland.

NOVEMBER 12. Grafton State Hospital, North Grafton.

DECEMBER 10. Worcester City Hospital, Worcester.

JANUARY 14. St. Vincent Hospital, Worcester.

FEBRUARY 11. Worcester State Hospital, Worcester.

MARCH 11. Memorial Hospital, Worcester.

APRIL 8. Hahnemann Hospital, Worcester.

MAY 13. Annual meeting, Worcester Country Club, Worcester.

## WORCESTER NORTH

OCTOBER 22. State Hospital, East Gardner.

JANUARY 28. Leominster Hospital, Leominster.

APRIL 22. Burbank Hospital, Fitchburg.

JULY 22. Henry Heywood Memorial Hospital, Gardner.

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NUMBER 13

## FRACTURES OF THE FOREARM AND ELBOW IN CHILDREN\*

An Analysis of Three Hundred and Sixty-Four Consecutive Cases

AUGUSTUS THORNDIKE, JR., M.D.,† AND CHARLES L. DIMMICK, JR., M.D.‡

BOSTON

IN making a study of children's fractures, one cannot but realize that growing bone, epiphyses and the extraordinary power of repair are major factors to be considered. However, there is no reason because of this reparative power that the surgeon or medical man treating these cases should be satisfied with a poor anatomic reduction. One often hears it said that if half the surface of a fractured bone fragment is in apposition, Nature will produce a satisfactory result. With the growing demand of the public for better medical and surgical care, it behooves physicians to be satisfied only with the product of their very best effort. Today, there should be no half way measures in fracture therapy.

The subject of this communication covers an important region of the child's body, a region involved most commonly in fractures. Beekman and Sullivan<sup>1</sup> report, in a series of over 2000 fractures in children, that 75 per cent were in the long bones of the upper extremity and that the radius was the most frequently fractured long bone in the body. The clavicle has usually been considered to be commonly injured, but it represented less than 8 per cent in their series. Figures will doubtless vary in different age groups of children, the clavicle being certainly the most commonly fractured bone at birth.<sup>2</sup> However, this paper is concerned with the age group from one day to twelve years.

During the last three and a half years, 364 consecutive cases of fracture of the forearm or elbow have been treated at the Children's Hospital. Of

these, the distal third of the forearm was involved in 200 cases, the middle and proximal thirds of the forearm in 58, and the elbow, including the head and neck of the radius and olecranon, in 106. From this series, dislocations of the distal radial epiphysis are omitted, being more properly included in wrist rather than forearm fractures.

In the treatment of fractures in the growing child, one should always be guarded in giving a prognosis, particularly when injuries to the epiphyses are involved. Aitken<sup>3</sup> has analyzed these fractures and has drawn some good conclusions. Abbott<sup>4</sup> has ascertained by a practical arithmetic formula the expected growth of a shaft attached to a damaged epiphysis. To interfere with normal growth, the fracture must pass through the cartilage plate and injure the proliferating cells. Separation of an epiphysis does not ordinarily injure these cells.

### FRACTURES OF DISTAL THIRD OF FOREARM

The character of bone in the growing child is such that a long bone fracture is often incomplete. In this series of 200 cases of fracture of the distal third of the forearm, 102 (51 per cent) had incomplete fractures, either subperiosteal or true greenstick in character, of 58 cases with fracture of the middle or upper third of the shaft of the forearm, 16 (28 per cent) had incomplete fractures, and of 106 cases with elbow fractures, 23 (22 per cent) had incomplete fractures. Thus, it appears that the more distal the fracture of the forearm, the greater is the likelihood of an incomplete fracture.

The treatment of these incomplete fractures is aimed at restoring proper anatomic alignment. A simple subperiosteal crack or impaction where the alignment remains normal needs no manipulative correction, merely fixation. The greenstick

\*Presented at the annual meeting of the New Hampshire Medical Society, May 13, 1941.

†From the Children's Hospital and the Department of Surgery, Harvard Medical School.

‡Associate in surgery, Harvard Medical School; associate surgeon, Children's Hospital.

§Associate in surgery, Harvard Medical School; resident in surgery, Children's Hospital.

shaft fracture with angulation requires manipulation, and often sufficient force to break the shaft completely through, to attain alignment, before fixation is applied. There are exceptions, however, even to this—notably greenstick fractures of the clavicle.

The necessity for surgical intervention in the treatment of fractures in this region should be determined by judgment acquired by experience. Beekman and Sullivan,<sup>1</sup> Whipple and St. John,<sup>5</sup> Ashurst<sup>6</sup> and Bosworth<sup>7</sup> agree that open reduction is rarely indicated. However, when necessary, it should be performed within forty-eight hours of the failure of closed reduction, with meticulous aseptic technic and with a minimum of trauma. At the Children's Hospital, we have never resorted to the use of bone plates, screws or other forms of advertised hardware; a reposition of fragments and periosteal suture, and occasionally wire suture, are employed. In only 2 (1 per cent) of the cases with fracture of the distal third of the forearm, six weeks and three weeks old, respectively, was open reduction necessary.

The art and science of closed manipulative reduction followed by proper fixation seem to be fast disappearing from the present era of surgical development. Admittedly, not all fractures can be adequately reduced by closed reduction, but the temptation to obtain anatomic alignment by open reduction is great in this age of gadgets. The aim of treatment is perfect function and as nearly as possible anatomic realignment and continuity. However, malunion and nonunion require all that surgical skill can provide—a different phase of fracture therapy. Compound fractures require careful débridement and surgical care. As yet, we have not adopted the Orr<sup>8</sup> or Trueta<sup>9</sup> method and can report that our 2 cases of compound fracture in this series (both in the distal third of the radius) healed by primary union.

The treatment that we recommend consists in early closed reduction, followed by adequate fixation. In fractures of the distal third of the forearm, not a Colles in children, some resort to the fluoroscope as an aid, but the cautious technician uses this piece of apparatus very seldom. Digital palpation and observation should assist one in ascertaining the proper alignment, and fixation should be promptly applied. X-ray films must be taken promptly after reduction and the application of fixation, not only to satisfy the surgeon of his manipulation, but also to serve as a safeguard against possible future litigation. Fixation is usually applied with molded plaster splints with the hand in semipronation; the plaster is carried around the elbow in true "sugar-tongs" fashion if it is

believed that the mobility of the upper fragments should be limited (Fig. 1).<sup>\*</sup> Board splints are still used, and give excellent results when properly applied.

When these patients are ambulatory in a sling,

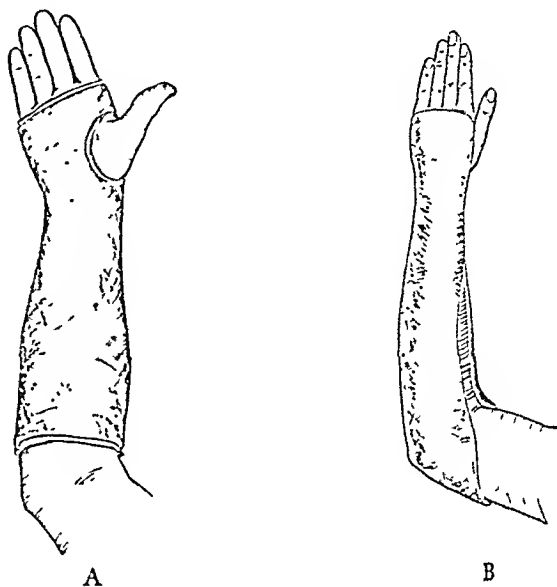


FIGURE 1. Fractures of the Distal Third of the Forearm Treated with a Molded Plaster Splint.

A cylinder is used in A, and a typical "sugar tong" in B.

one should follow them at least twice a week, removing and repadding and adjusting the splints at regular intervals. The posterior splint should be removed after three weeks, the anterior splint after four weeks, and the sling after six weeks.

TABLE 1. Results of Treatment in Fractures of the Distal Third of the Forearm.

TYPE OF FRACTURE	NO. OF CASES	CASES REDUCED	RESULTS	
			GOOD	IN-ADEQUATE FOLLOW UP
Both bones (incomplete)...	42	31	27	15
Both bones (complete).....	56	52	40	16
Radius (complete) and ulna (incomplete).....	9	8	6	3
Radius (incomplete).....	49	16	39	10
Radius (complete).....	31	20	26	5
Miscellaneous (subperiosteal)	13	0	11	2
Totals .....	200	127	149	51

In our series, there were 9 cases of refracture between one month and five years following the original injury.

Table 1 presents the results of treatment in fractures of the distal third of the forearm.

#### FRACTURES OF PROXIMAL TWO THIRDS OF FOREARM

In fractures of the proximal two thirds of the bone shafts of the forearm, early reduction and

<sup>\*</sup>Surgeons experienced in the use of the more recently developed plastic materials (Castex and Thermex) may substitute these light waterproof molded splints for plaster of Paris.

adequate fixation are essential. Careful closed manipulation, with fluoroscopy as an aid, must be promptly carried out. In this portion of the forearm, palpation is less accurate, and x-ray visualization is of value. Whipple and St. John<sup>5</sup> have

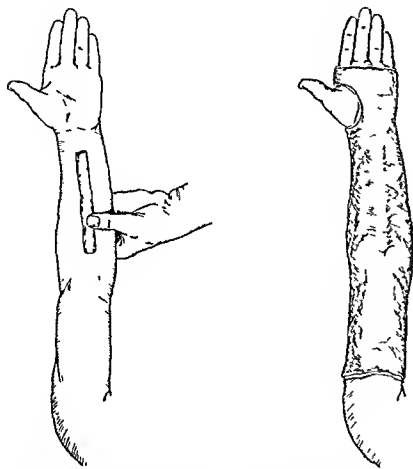


FIGURE 2. The Use of a Plaster-Bandage Roll, over the Flexor Surface of the Forearm, as an Extra Aid to Fixation in Fractures of the Proximal Two Thirds of the Forearm

recommended full supination of the hand as the position for fixation, with the elbow flexed to 90°, and an internal angular splint of metal. Plaster of Paris is now the customary splinting material, and is put on as a full cylinder from the knuckles

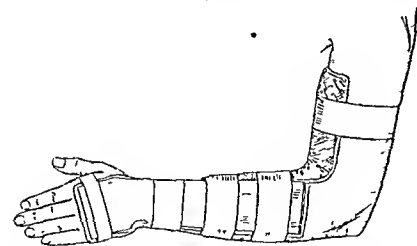


FIGURE 3. The Use of Internal Angular and Board Splints for Immobilization of Fractures of the Proximal Third of the Forearm.

Supination rather than the neutral position may be substituted.

to the axilla, with the hand in supination and the elbow in extension or in right-angle flexion (Figs. 2 and 3). It is impossible to set any hard and fast rule for the latter, because no two cases are exactly alike and each is an individual problem.

Flexion will hold some, but not all. The use of a narrow roll of plaster bandage placed between the layers of plaster on the flexor surface of the supinated forearm in the area of the interosseous membrane does assist in holding these bones in alignment. A sling is used when the elbow is fixed at 90° flexion.

It is best to leave the original plaster for three or four weeks and then secure partial immobilization in molded plaster splints for another two or three weeks. Beekman and Sullivan<sup>1</sup> recommend fixation for eight weeks, because of the apparent likelihood of refracture. Although this period seems long to us, it is safe, but will not prevent all refractures. Our series of 58 patients

TABLE 2. Results of Treatment in Fractures of the Proximal Two Thirds of the Forearm.

TYPE OF FRACTURE	NO. OF CASES	CASES REDUCED	RESULTS	
			GOOD	IN-ADEQUATE FOLLOW UP
Both bones (incomplete)	10	10	5	5
Both bones (complete)	28	28	26	2
Radius (complete) and ulna (incomplete)	3	3	3	—
Radius (incomplete)	5	5	4	1
Radius (complete)	6	4	6	—
Ulna (incomplete)	1	—	—	1
Ulna (complete)	5	5	3	2
Totals	58	55	47	11

with fractures of the upper two thirds of the forearm includes one with refractures at the original site three times in three years, 2 cases with refracture in two years, and 4 cases with refracture between three months and thirty-three months after the original injury. Of this entire group, not one case required open reduction. On the whole, the results of this method of treatment are entirely satisfactory (Table 2).

#### FRACTURES OF ELBOW

In fractures of the elbow, particularly those of the distal end of the humerus, one should follow the principles set down by Ashurst<sup>6</sup> in 1910 and emphasized again by Ladd<sup>10</sup> in 1916. The results are surprisingly good with conservative treatment, although one should remember that if premonitory signs and symptoms of Volkmann's ischemic contracture appear within the first twenty-four hours, the fracture should be "taken down," the skin prepared, and open reduction and evacuation of the hematoma performed within forty-eight hours. In all types of fractures, Ashurst with 56 cases had 81 per cent "perfect" results, and Ladd with 45 cases had 91 per cent. In the purely supracondylar and transcondylar types, their results are even better. The problem comes down to a definition of the adjective "perfect." We consider that perfect function entails no greater total loss of

combined flexion and extension than  $10^{\circ}$  (a maximum limitation of  $5^{\circ}$  each), with normal supination and pronation and a carrying angle with a cubitus varus or valgus of only slight degree if any. Since there is a variation in elbow function in every person, one must compare the patient's normal elbow with the injured when arriving at any definite conclusion. A skillful reduction must be performed early, before too much swelling is

pletely. It undoubtedly might be a useful method in fractures that are badly swollen, with blebs in the skin, and those that are twenty-four hours old.

In supracondylar and transcondylar fractures of the humerus, the reduction is carried out under a general anesthetic by a gentle rocking motion of the elbow in hyperextension, properly to align and engage the fragments in the anteroposterior plane, and then hyperflexion so that the fingers of the

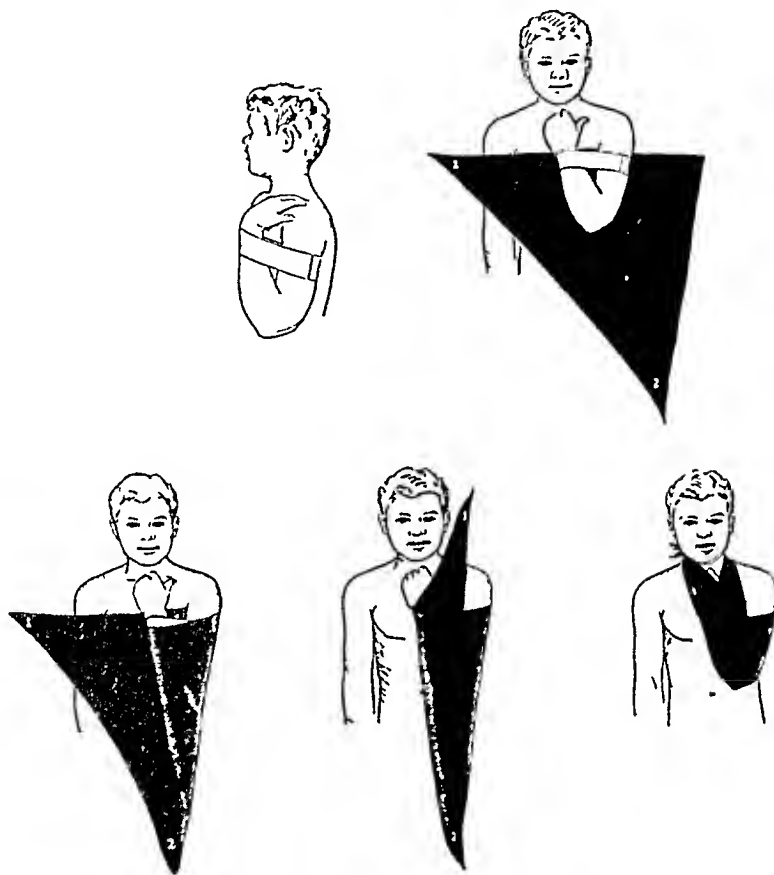


FIGURE 4. *The Acute Flexion Position for Fractures of the Elbow, except Those of the Olecranon, Using Adhesive-Tape Fixation, with the Pistol-Holster Sling.*

apparent, and the fixation must hold the reduced fragments in position.

As a general rule, we use the acute flexion position in all elbow fractures except those of the olecranon. We maintain the position by the use of adhesive plaster and the so-called "pistol-holster" sling (Fig. 4), thereby leaving the fingers, hands and radial pulse readily palpable. By untying the sling from behind the neck, the elbow itself is made visible without loss of the fixation. All patients with elbow fractures should be hospitalized for at least twenty-four hours after reduction. Dunlop<sup>11</sup> has described a method of adhesive bed traction with which we have had no experience, but according to Ashurst<sup>6</sup> this should not reduce the distal fragment of the transcondylar type com-

hand rest on the acromioclavicular joint of the shoulder. The arm is held in that position while the bony landmarks are identified and compared with those of the normal elbow in hyperflexion and while the circulation in the fingernails and radial pulse is checked. If reduction is incomplete, the fingers will not rest on the shoulder, and the radial pulse will be lost and the maneuver must then be repeated, thumb pressure on the distal fragment being exerted during the flexion stage. Fluoroscopy is of considerable assistance in cases presenting marked swelling. The maneuver does not require force to attain reduction. Once the adhesive-tape fixation is applied, x-ray films should be taken in both planes, and if the position is good, the pistol-holster sling is applied and



the child put to bed. The postoperative orders should require an hourly check on the pulse and circulation of the wrist, hand and fingers. Among the 58 reductions of transcondylar and supracondylar fractures of the humerus, there was 1 open reduction; furthermore, in 20 of these cases, there was gross displacement, usually medial and posterior, of the distal fragment.

The reduction of fractures of the lateral and medial epicondyles and of the T fracture should be manipulated in much the same way, but one should rely more on digital pressure to replace them. The badly displaced fractures are difficult and require operative reduction and suture in position. Beekman and Sullivan<sup>1</sup> do not hesitate to operate because the carrying angle is so affected by an improperly replaced condyle. With the acute flexion position, it is the tightly drawn fascial envelope of the triceps muscle that holds these fragments in place. Guarded prognoses should always be given in these cases, because the epiphyseal cartilage plate has been damaged.

Fractures of the head and neck of the radius enter the joint, and radical surgery (excision of the head) in a growing child always results in a crippled elbow joint. The healing that takes place in a slightly displaced head of the radius is remarkable, provided the two fragments touch at all, and it is preferable to be ultraconservative. In this series, we had 3 cases of complete displacement of the head from the neck of the radius.

Olecranon fractures in children are rarely complete, with separation of the fragments. This occurred in none of the 4 cases in the series. If separation occurs in the growing child, however, we prefer operative reduction and suture of the overlying fascia; no hardware should be used.

When acute flexion position is utilized, this position and fixation should be maintained for three weeks; of course, the skin should be checked and cared for twice a week during that period. For the following week, a triangle sling is used under the clothing, and the elbow carried at 90° flexion. For the fifth week, the sling is carried outside the clothing, and at six weeks the arm is free. Physiotherapy should never be employed in the convalescent care of elbow fractures in children, and Nature should be allowed her opportunity to absorb excess callus and to improve motion. Forced manipulation should never be used in an attempt to increase motion. End results are not always obtained until eighteen to twenty-four months after the original fracture.

The end results of the 106 fractures of the elbow treated according to these general principles are presented in Table 3. Of the unsatisfactory results

in 8 cases, the fractures were in the head and neck of the radius in 2, in the region of the lateral condyle in 3 (2 of these were old united fractures when the patients came to the hospital and had originally been treated elsewhere), supracondylar in 2 (1 of which was a month old on entry), and an old transcondylar fracture in 1. Therefore, excluding the old fractures, there were 5 unsatisfactory end results in 98 cases of elbow fracture, or an incidence of 5 per cent.

One should face the problem of elbow fractures in children with meticulous care and courage, for

TABLE 3. *Results of Treatment in Fractures of the Elbow.*

TYPE OF FRACTURE	NO. OF CASES	CASES REDUCED	RESULTS		
			GOOD	POOR	INVALIDATE FOLLOW-UP
Transcondylar (humerus)	50	47	45	1	4
Supracondylar	12	11	8	2	2
Lateral condyle and epicondyle	21	21	17	3	1
Medial condyle and epicondyle	7	7	7	—	—
T	2	2	2	—	—
Head and neck of radius	10	10	7	2	1
Olecranon	4	4	4	—	—
Totals	106	102	90	8	8

on the whole the results are quite satisfactory. The problem of operative correction of bony deformity in a healed elbow fracture is tempting, but it is a better policy to await the full growth of the child before such corrections are attempted. To damage the growing cartilage plate by operative interference because of a false carrying angle or prominent condyle is foolhardy, meddlesome surgery.

In this series of 106 fractures of the elbow in which 102 reductions were carried out, there were

TABLE 4. *Results of Treatment by Open Reduction in Fractures of the Elbow.*

TYPE OF FRACTURE	NO. OF NEW CASES	NO. OF OLD CASES	RESULTS	
			GOOD	POOR
Transcondylar	1	1	1	1
Lateral condyle and epicondyle	1	1	1	1
Medial condyle and epicondyle	1	—	1	—
Head and neck of radius	5	—	4	2
Totals	6	2	4	4

8 open reductions after attempted closed reduction had failed. The results are given in Table 4. Open reduction was attempted in two old fractures (more than one month after the injury), and in each case there was a poor result. Two out of 3 cases of fractures of the head and neck of the radius with displacement of the fragments resulted poorly. From this small incidence of open

very meager, but in self-sacrifice, nobility of character and wisdom he was in truth a giant.

If I could bring home to you in this dissertation only one sustaining inspiration, it would be the cultivation of the broad understanding that characterized those benevolent family doctors. I am sure, by and large, they never thought in terms of an ethical code, but rather lived their private, as well as their professional, lives in an honorable relation to fellow practitioners and patients. Consequently, the thought that is uppermost in my mind in dealing with medical ethics is, somehow or other, to get you to think of the code, not as a set of rules and regulations, like the by-laws of a state medical society, but rather as professional ideals of duty and obligation.

You will learn, when you get time to indulge yourself in the luxury of reading medical history, that medical ethics go back to the year 2250 B.C. when a Semitic king, Hammurabi, in Babylon, chiseled out a code of ethics on stone tablets. You will often be reminded of the Oath of Hippocrates, which for 2400 years has been the pledge of physicians. How else can we explain the virility of these principles and precepts, which are self-imposed, except by saying that they are based on truth? And may I now remind you that you will soon enter the portals of a profession that has unswervingly adhered to its nobility of purpose since the very beginning of its existence?

I think it would be well to take the time to quote this oath. You may be familiar with it, although I cannot recall having heard it until the day of graduation, and I think the wise and prudent, though departed, Dr. George W. Gay, who sponsored this lecture, expects it. Let me read it to you.

I swear by Apollo, the Physician, by Aesculapius and Health, and All-heal, and all the gods and goddesses, that, according to my ability and judgment, I will keep this oath and stipulation,—to reckon him who taught me this art equally dear to me as my parents, to share my substance with him and relieve his necessities if required; to regard his offsprings as on the same footing with my own brothers and to teach them this art if they should wish to learn it without fee or stipulation; and that by precept, lecture and every other mode of instruction I will impart a knowledge of the art to my own sons and to those of my teachers and to disciples bound by a stipulation and oath according to the law of medicine, but to none other.

I will follow that method of treatment which according to my ability and judgment I consider for the benefit of my patients and abstain from whatever is deleterious and mischievous. I will give no deadly medicine to anyone if asked, nor suggest any such counsel, furthermore I will not give a woman an in-

strument to produce abortion. With purity and with holiness I will pass my life and practice my art. I will not cut a person who is suffering with a stone but will leave this to be done by practitioners of this work. Into whatever houses I enter I will go into them for the benefit of the sick and will abstain from every voluntary act of mischief and corruption and further from the seduction of females or males bond or free.

Whatever in connection with my medical practice or not in connection with it I may see or hear in the lives of men which ought not be spoken abroad, I will not divulge as reckoning that all such should be kept secret. While I continue to keep this oath unviolated may it be granted to me to enjoy life and the practice of the art respected by all men at all times, but should I trespass and violate this oath may the reverse be my lot.

Certainly these are broad principles of moral conduct from the greatest physician of ancient Greece, and you will do well, in your early days of practice, when unwanted leisure may tempt you to much profitless reading, to study his life and writings. I shall not burden you with many references but would recall that he was the first actually to differentiate diseases and by accurate observation and study to divorce sickness from superstition.

Coming down somewhat closer to our time, you will find a book published in 1803 and written by Dr. Thomas Percival to be most eloquent. This is entitled *Medical Ethics: A code of institutions and precepts adopted to the professional conduct of physicians and surgeons*. From this delightful book, which I recommend to you, is derived the code of ethics of the American Medical Association.

Carefully weighing these many admonitions laid down for us in the code and in the great writings of the master minds of medical history, we find constantly re-emphasized the physician-patient relation and the ever-present reminder that our first duty is to our patients. Certainly, you have a duty to other members of the profession, to the public in general and to yourself. Of these, I shall also have something to say presently, but they naturally follow the other in the order of their importance.

Somewhere in my early medical days,—just when or where, I cannot be sure, but probably from Dr. William H. Robey, whose kindly wisdom, advice and guidance, and example did much toward shaping my own career,—I learned that the treatment of a disease is wholly impersonal but that the treatment of a patient is entirely personal, and that a great physician combines in himself the utmost in scientific knowledge and the quality of complete self-sacrifice. Not so long ago I had the pleasure of discussing some of these qualities with Dr. Soma Weiss, who gave it as

his opinion that the basic elements of greatness were "sincerity and genuine sympathy."

Here I need not dwell on your broad training in the medical sciences, which has been well attended to, but I have found in my years of contact with interns that there is often a sad lack of training in the virtues of tolerance, patience and sincerity. The old notion that physicians are born has almost disappeared. They are not born, they are trained, and they are trained for the care of the sick. The attribute of a self-sacrificing desire to restore health as completely and as quickly as possible has characterized all the great doctors of history, even down to this very day, and when you receive your degree in medicine there goes with it this responsibility to the sick.

Not all of you will have the two important prerequisites for greatness in the same proportion. With some it will be more science and with others more art. Accordingly, I should not say that with science alone you cannot be great, for there may be those among you who will go into fields of research and pure scientific investigation, those whose careers completely separate them from the care of the sick, those whose names may shine as brilliantly as that of the late Dr. Frederick G. Banting, who gave us insulin for diabetes. But I most sincerely assure you who will be practitioners that the measure of your success depends ultimately on with what measure of both these components you are blessed.

I suppose one of the most puzzling questions that you as young practitioners will ever ask, your selves will be, How do people pick out a particular physician? or How did so and so ever happen to call me? I have no clear cut answer for these questions. I have long thought about this and tried to evaluate the various elements involved. Salesmanship—and I mean the ability to sell yourself—seems very important. Personality, in the sense of the sum total of character must be equally important, although I am sure that ability and skill may, sooner than you would believe, become the determining factors.

Probably your first actual responsibility to a sick person will come in the hospital wards and a problem that has often come to my mind of late has to do with your handling of patients in house officers, during either your internship or residency. Here I admonish you not to say things, publicly or in the hearing of others, that will hurt the feelings of your patients or frighten them for it serves no good purpose other than to mark you as lacking in kindness and sympathy.

Because of their teaching value, clinics and ward

rounds have become very general, even in the small hospitals widely separated from medical schools. If carefully considered, they can be conducted without emotional damage to the patient, although not always, I fear.

I had a recent experience in a large metropolitan teaching hospital that makes this point clear. I was there for a brief visit with the chief in medicine, one of our greatest present day internists, he turned me over for a short ward round with one of the younger members of his teaching staff, who appeared to be very familiar with his cases and well informed medically. However, he talked freely and openly. It was not a large ward, and everyone in the place knew the most intimate details of the other's histories, both medical and social, except for that of one timid woman of about fifty-five. She was in the next to the last bed, and when we came up to it, the intern gave me her clinical record and pointed to the x-ray report, which showed extensive cancer of the stomach. He said not one word about the case and continued on to the last patient, but his silence was infinitely more eloquent than his previous discussion of the other cases. As he put the record back on the foot of the bed and was about to go on, the poor woman broke into tears and cried out, 'Oh, I am sure I have some terrible disease because you always tell about the others and then whisper about me.' It was no easy job for this physician and myself to quiet her down, and I am sure that we did not begin to undo the damage my visit had caused.

Let you think that this question of the patients' emotional reactions to their examinations on rounds and at clinics is one of very minor importance, I might tell you that at this time in more than one of our major teaching centers, a very serious study of just this problem is being made.

The matter of consultations should find a place in the early part of this presentation because you will not be long, in practice before you will come face to face with this aspect of medical life. You will find a great divergence of opinion among your confreres on the subject, and I can serve you best by presenting it from a personal point of view.

As your years in practice increase, you will most surely fall into one or the other of two general groups: those who seek and desire consultations, and those who spurn and abhor them. It is my counsel that you be in the first group. Confronted with a serious situation, do not risk carrying the entire responsibility, share it with some consultant, preferably one of your own choice. Ask for the

general practice, you will most probably find the office and house fee a well-settled local custom, long before your arrival. In the special fields, this is also true, although in surgery the situation is more flexible. The honorable surgeon will set a fee somewhat according to the patient's means, and this is equally true of consultations. Often it is my custom to ask the doctor who calls me about the family circumstances and even to let him suggest the fee. I do not feel too strongly about this plan, however, for often he sets too low a valuation on the consultation, and experience will teach you that many people value your services at just the price you put on them. Contrasted to this, however, you will find among your true charity cases and your free-ward cases in the hospital those who set a value, much beyond price, on what you do for them. It is an open question to what extent a large income elevates a professional man and to what extent a generally high level of income elevates the whole profession. Material prosperity should be valued in its proper perspective.

Now let me turn from this consideration of duty to your patients and duty to your professional brothers to that of the public in its larger sense. It is not in my mind to discuss public service as it applies to a health officer, a medical officer of the United States Army or Navy or an official of a corporate or tax-supported institution or government department, but specifically, to dwell for a few moments on another aspect of the life of the practitioner.

In alluding to some of these, it might be well to dispose first of a question often raised by the laity and to some extent believed by them, namely, Is a physician legally obliged to respond to a professional call from anyone? If the call comes from complete strangers, or from those whom you never previously attended for an illness that might be linked to this call, it may be unreservedly stated that you have no responsibility to accept such a case. But should you choose to go in response to such a summons and engage in the case, you do acquire a legal responsibility, for you have become a party to an implied, even though unwritten, contract, and you will be subject under all the laws and statutes applicable to contracts, even to defending yourself in a court of law for any breach thereof. This being so, there remains, nevertheless, the certainty that the true physician has ever been ready and willing to respond in an emergency, for it is quite obvious that any physician would be more helpful than a lay person, even those who have for years limited their practice and studies to a special branch. Such a situation was my experience a few years

ago when I came on the scene of an automobile accident and found the person who was adjusting a pillow and side splint to a fractured lower leg to be the senior eye specialist of our hospital; in talking it over with me later, he told me what a pleasure he got out of doing it, although I am sure he never learned the victim's name, much less got a fee for his trouble.

Another duty to the public on which I am inclined to dwell somewhat, is one, if you will permit me to say so, with which I have had considerable experience. It is your appearing before courts of law and boards of adjudication. This is a duty that you cannot hope to escape, for on a day when it seems that nothing more can be heaped on you in the way of other people's troubles, there will come into your consulting room a large and rather sober-looking man. Just as you are about to offer him your comfortable desk-side chair and ask him his name for your clinical record, he will reach into an inside pocket and produce, like a rabbit out of a hat, a court summons demanding your appearance in court at 9 a.m. the next day. This hour, curiously enough, will be the very time you had reserved at the hospital for a tonsillectomy.

Few of you who are going into general practice, or even the specialties, will have quite enough of this to give you a feeling of being at home on the witness stand, and since it is a matter of some importance to your pride that you acquit yourself with credit, both personally and professionally, I venture this concise advice: be scrupulous in your honesty. No doctor on the witness stand who keeps this in mind is ever in trouble, although I concede the difficulty of not being biased, either for your patient or for the insurance company that employs you. To this might be added the desirability of keeping your answers as simple as the purport of the query permits, the uselessness of volunteering information not asked for and, finally, the value of preparing yourself for testifying by familiarizing yourself with the factors involved, as they relate to medicine in general and the case in particular. It matters little how clever and menacing the cross-examiner; he is a lawyer, and although he may have a well-deserved legal reputation and a large medical vocabulary, you are a physician, skilled in the field about which you are testifying, not deviating from the known facts, and not afraid to say, "I don't know."

It was my good fortune very early in my medical life to have had a word of advice on this matter from Dr. Timothy Leary. While I was a house officer at the Boston City Hospital, an unconscious patient was admitted who obviously was

dying of meningitis. A lumbar puncture proved it to be a pneumococcal meningitis. We had no serum or sulfathiazole in those days, and the patient died in a few hours. It so happened that the patient had been in a street fight the previous day, and on this basis it became a medico-legal death; Dr Leary, who was the medical examiner, autopsied the man and found a skull fracture through the temporal bone and the probable point of entry for the pneumococci. The other details are unimportant, but there was a political angle to the case, and it finally developed into a charge of manslaughter. Presently I was summoned into court; this was my first experience, and you may rightly suspect that I was nervous, because my testimony was important in linking this death with Dr. Leary's findings. When I met Dr. Leary in the corridor of the courthouse, I told him how nervous I was and asked him what advice he could give me, since it was my first appearance in court as a witness. His counsel I pass on to you: "Tell the truth and don't deviate from it, no matter what they ask you. If you don't know, say so; don't quibble and don't split hairs."

It is probable that in the course of your practice, you will often be called on for health certificates, disability statements and compensation forms, and, at the moment, there are those who seek a statement that they have a disability that will exempt them from military training. Surely by now, there is nothing for me to add in this regard, for your self-imposed rule of conduct in all your dealings with your fellows will be the guide.

It may be that I should add a word or two about advertising, which, I believe, is in much the same position as fee splitting. In New England it just is not done, or if it is, it has quite escaped my observation. You may occasionally need a modest and dignified notice in the local paper on your return to practice following a reasonably long absence, and this is quite proper; but conscious and deliberate advertising should be generously left to the cultists and quacks.

Publicity seeking, however, is quite a different matter and a much more insidious disease. In calling your attention to it, let it be assumed that you recognize I allude to the pursuit of this siren, who may well lure you from your high purpose to the rocks of mediocrity. Your measure of greatness may well be the relative rarity with which your name appears in the daily press and the frequency of its appearance in the *Quarterly Cumulative Index*. In no sense does this statement imply that when you have reached a

position of prominence and importance in your community you will demand anonymity; rather, it is my hope that it will suggest which of these two points of view has in it attributes of greatness. You will be expected, from time to time, to lend the authority of your name to a radio talk, which, when properly sponsored, is completely ethical; in fact, it might rightfully be considered among your duties to the public, for we are the ones to educate laymen in matters that pertain to their health. It is a vast and tremendously interested audience that listens to physicians on the radio. If kept within proper limitations, this activity does much to counteract the mischief of the cults.

Passing from these responsibilities to the public, consider with me the more intimate and personal aspects of medical life, which I have chosen to call "duties to yourself." The public will demand much of you, organized medicine its share, and your patients practically all of you; therefore, it is to those things that contrast you with others of our profession, also serving this triad of taskmasters, that I shall turn my attention.

I might enumerate a long list of "don't's," such as dressing flashily, driving around in a brightly automobile and not keeping your person and office businesslike, but I incline to the general belief that you are well informed on these matters from your own observation and general knowledge. Furthermore, I do not intend to spend much time in stressing the importance that attaches to the possession of a good professional manner. This you will acquire in just the right proportion, as you respect the dignity of your calling. Perhaps the Vandylke beard and the Prince Albert coat did enhance the professional air of those doctors of a former generation. However, I think you need not worry about acquiring a silk hat as a badge of your profession, lest your patients think that you have just dropped in on your way to a wedding or a funeral.

My concern is more with your acquiring a continuing medical capacity. You have, by now, become aware of the inescapable fact that medical knowledge is never static, that many times you must unlearn and relearn the management of a given disease, in the light of new information and discoveries. If you review the papers written on diabetes by such an authority as Dr. Elliott P. Joslin, in the space of his professional experience, you will see the truth of this statement.

Presently many of you will be starting or seeking internships. In my medical school days only a part of the graduates took intern training. I

## DISSECTING ANEURYSM OF THE AORTA

## Report of a Case

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DISSECTING aneurysm of the aorta was first described more than two hundred years ago by a British physician named Nicholls,<sup>1</sup> who demonstrated in 1728 that rupture of the inner coat of the aorta could occur without rupture of the outer coat, an aneurysm developing within the middle layer. The same physician in 1761 performed an autopsy on the body of King George II, of England, who had died suddenly while straining at stool. Nicholls found a dissecting aneurysm of the aorta, which by pressure on the pulmonary artery had caused rupture of the right ventricle and sudden death. The great anatomist, Morgagni,<sup>2</sup> recognized dissecting aneurysms and described an autopsied case as early as 1769. A striking account of a dissecting aneurysm occurring during labor was reported by Lynn<sup>3</sup> in 1798. The master French clinician, Laënnec,<sup>4</sup> was familiar with this condition, to which he applied the term, "aneurysma dissecans," in 1819. The first correct ante-mortem diagnosis was made in 1856 by Swaine.<sup>5</sup>

Although 500 cases of rupture of the aorta appeared in the literature during the next eighty years, in only 9 was a correct ante-mortem diagnosis made until the subject was carefully reviewed by Osgood et al.,<sup>6</sup> and by Peery<sup>7</sup> in 1936 and independently studied a year later by McGeachy and Paullin,<sup>8</sup> who reported 3 cases of their own, with correct diagnosis before death. As a result of these recent analytic clinical studies, interest in the condition has received renewed impetus during the last three or four years, and reports of accurate ante-mortem diagnoses are no longer a rarity. However, since dissecting aneurysm of the aorta is found with increasing frequency and since this condition may be readily confused with coronary thrombosis, we believe that a short outline of the clinical features of dissecting aortic aneurysm, with an illustrative case diagnosed on the first day of the disease, will not be amiss.

The clinical picture may be confusing because of the severity of the onset, which may make a detailed examination impossible, and because of the rapid sequence of alarming symptoms, which

spell a fatal termination in twenty-four hours or less in more than 75 per cent of the patients. Sudden death is almost a common denominator and often occurs before diagnosis can be made. More recently, a chronic form of the disease, presenting symptoms of progressive decompensation simulating cardiovascular syphilis, has been recognized. In 4 such cases reported by Gouley and Anderson,<sup>9</sup> the patients did not complain of any pain whatever during the entire course of their disease, which varied in duration from two months to four years.

A dissecting aneurysm develops as a result of the rupture of the intimal lining of the aorta a short distance above the valve ring, either at the site of an arteriosclerotic plaque<sup>7</sup> or at the locus of rupture of one of the vasa vasorum.<sup>10</sup> In either event, the lesion is associated with arteriosclerotic or cystic changes in the elastic tissue of the media (necrosis media aortica cystica).<sup>11</sup> Degeneration of the media, possibly owing to metabolic toxins, leads to intramural changes and thus paves the way for dissection by the aneurysm.<sup>12</sup> This condition is not limited to the aorta alone, since it is primarily a disease of blood vessels with elastic tissue and may therefore appear in the subclavian or iliac arteries, or both. Blood from the lumen is forced through the tear in the intima into the medial coat, where dissection begins at once and progresses very rapidly depending on the height of the systolic pressure and the extent of the cystic degeneration of the elastic tissue in the middle third of the media. The sudden rupture of the intima, with tearing of the medial coat of the aorta, permits the blood to dissect its way between the layers of the media along the entire course of the aorta or outward within the medial coat of the subclavian arteries or downward within the iliac arteries.

This aneurysmal extravasation of blood under high pressure is usually precipitated by emotional excitement or sudden physical exertion. The onset is accompanied by exquisite pain and often by extreme shock, which in itself may be fatal. At first the pain is either thoracic or epigastric, then rapidly spreads downward to the lower abdomen or to the lumbar region and the legs. Vomiting may be associated with the epigastric

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pain, but usually there is little or no abdominal rigidity. As the aneurysm dissects its path between the coats of the aorta, impairment of the circulation to and from the adjacent viscera gives rise to a host of symptoms. Cyanosis and engorgement of the thoracic veins may result from pressure of the aneurysm on these blood vessels. Inefficiency of the cerebral circulation may be noted, owing to involvement of the carotid or innominate arteries. Inequality of the blood pressure may occur in the two arms. Paralysis of the left recurrent laryngeal nerve is not uncommon; dysphagia due to esophageal pressure has been re-

ported. Dyspnea resulting from crowding of the left lung is a fairly frequent finding. Left-sided pleural effusion or collapse of the left lower lobe may occur because of pressure of the aneurysm in this region. Partial occlusion of the renal arteries often gives rise to hematuria, followed by anuria. Further dissection of the aneurysm downward toward the iliac region embarrasses the peripheral circulation in the limbs, as shown by progressive failure of motor power in the lower extremities. The pulsation of the dorsalis pedis artery may be lost in one or both feet. Blood pressure readings in the right and left popliteal regions may show wide discrepancies. The legs become cold, cyanotic and flaccid. Gangrene has been reported as a terminal affair, although few patients live long enough to develop this complication. Impairment of the circulation of the lower extremities has been thought to be due to involvement of the lower intercostal and lumbar branches of the aorta to the anterior and posterior spinal vessels, the dissection thus interfering with the circulation of the spinal cord.<sup>13</sup> Inequality of the blood pressure determinations in the legs may result from constriction of the lumen of the iliac artery as the aneurysm dissects its way within and between the layers of the medial coat.

Aneurysm of the aorta is typically excruciating in character and may be described by the patient as a rending, tearing or rupturing sensation over the precordium, between the scapulas, in the neck, in the epigastrium or in the lumbar region. The pain spreads from the front to the back or vice versa, and usually from the chest to the abdomen and back and down the legs. Rarely does it radiate to the arms. In the atypical form, the "mystery" may be mild, indefinite and intermittent, or conspicuous by its absence.<sup>3</sup> On the other hand, the pain may be excruciating in character and entirely localized below the diaphragm, and may

TABLE 1. *Differential Diagnosis of Dissecting Aneurysm of the Aorta and Coronary Thrombosis*

SYMPTOMS AND FINDINGS	DISSECTING ANEURYSM	CORONARY THROMBOSIS
Onset	Sudden tearing, terrific	Oppression develops slowly
Occurrence	Exertion usually precipitates initial pain	May come on while the patient is at rest
Location of pain	High in chest behind sternum (may be entirely abdominal or referred only to the lower extremities)	Fairly low in the chest
Radiation of pain	To the back in the thoracic or lumbar region	To the neck and left inner arm
Cardiac friction rub	Absent	May appear in a few hours
Roentgen findings	Aneurysmal shadow (may extend along a cervical vessel)	Normal mediastinum
Heart	Usually enlarged (previous hypertension)	May be of normal size
Electrocardiography	Inconstant changes (if any)	Characteristic changes
Circulatory block of an extremity	Common but transient	Uncommon embolic and permanent
Central nervous system symptoms	Paralysis may be partial and progressive or complete (hemiplegia)	Absent; apprehension often a prominent feature
Pleural effusion	Fairly frequent	Very rare (except in chronic decompensation)
Vasodilator drugs	No effect	May relieve anginal syndrome

ported. Dyspnea resulting from crowding of the left lung is a fairly frequent finding. Left-sided pleural effusion or collapse of the left lower lobe may occur because of pressure of the aneurysm in this region. Partial occlusion of the renal arteries often gives rise to hematuria, followed by anuria. Further dissection of the aneurysm downward toward the iliac region embarrasses the peripheral circulation in the limbs, as shown by progressive failure of motor power in the lower extremities. The pulsation of the dorsalis pedis artery may be lost in one or both feet. Blood pressure readings in the right and left popliteal regions may show wide discrepancies. The legs become cold, cyanotic and flaccid. Gangrene has been reported as a terminal affair, although few patients live long enough to develop this complication. Impairment of the circulation of the lower extremities has been thought to be due to involvement of the lower intercostal and lumbar branches of the aorta to the anterior and posterior spinal vessels, the dissection thus interfering with the circulation of the spinal cord.<sup>13</sup> Inequality of the blood pressure determinations in the legs may result from constriction of the lumen of the iliac artery as the aneurysm dissects its way within and between the layers of the medial coat.

The initial pain associated with a dissecting aneurysm of the aorta is typically excruciating in character and may be described by the patient as a rending, tearing or rupturing sensation over the precordium, between the scapulas, in the neck, in the epigastrium or in the lumbar region. The pain spreads from the front to the back or vice versa, and usually from the chest to the abdomen and back and down the legs. Rarely does it radiate to the arms. In the atypical form, the "mystery" may be mild, indefinite and intermittent, or conspicuous by its absence.<sup>3</sup> On the other hand, the pain may be excruciating in character and entirely localized below the diaphragm, and may

thus present the clinical picture of an acute surgical abdomen.<sup>14</sup> But as a rule, a wide, rapidly progressing spread of pain is almost pathognomonic. Shock and collapse are common, and dissecting aneurysm of the aorta is a more frequent cause of sudden death than is generally realized.

This disease occurs usually after the age of fifty, oftener in men than in women, and is found in patients with high blood pressure and extensive arteriosclerosis. The average frequency of this condition at autopsy is 1 case in 630.<sup>15</sup> In the majority of patients, the blood pressure remains elevated throughout the disease, and the higher the degree of hypertension the more rapidly the aneurysm dissects its way downward along the aorta. The clinical picture often resembles the syndrome of coronary thrombosis, but the sudden and dramatic onset of thoracic pain and the persistent hypertension in the presence of shock should lead one to suspect a dissecting aneurysm of the aorta.<sup>16</sup> The x-ray, fluoroscopic and electrocardiographic findings aid in establishing the diagnosis if the patient is not too ill to submit to these procedures. If the patient is in extremis, the correct diagnosis may be most difficult. Indeed, the history alone may be of great value in such cases. When no accurate his-

tory is obtainable, one must consider and rule out pulmonary embolism, spontaneous pneumothorax, ruptured peptic ulcer, cholelithiasis, renal calculus, rupture of a mediastinal abscess and hemorrhage from a new growth in this area. Perforation of a saccular aneurysm and cerebral hemorrhage should not be lightly discarded from the examiner's mind. To clarify the situation, Table 1 presents an outline of the main points of difference between dissecting aneurysm and coronary thrombosis.

The following case illustrates some of these points, since the diagnosis was suspected a few hours after the onset of the initial attack and was confirmed by x-ray films and electrocardiograms later the same day. Post-mortem examination on the nineteenth day of the disease revealed a dissecting aneurysm of the aorta, with death due to rupture of the aneurysm into the left pleural sac.

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The admission diagnosis of coronary thrombosis was considered untenable because of the extreme severity and continuance of pain in spite of massive doses of morphine and the nitrites. Moreover, the persistent bradycardia and the hypertension in the presence of pronounced shock were very atypical of coronary thrombosis. Because of the general picture, the likelihood of a dissecting aneurysm of the aorta was suggested by his physician (C. C. S.) and the consultant (H. T. F.). This diagnosis was supported by an electrocardiogram, which was negative except for inversion of T<sub>1</sub> and by a roentgenogram (Fig. 1), which showed a probable dilatation of the descending aorta.

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and the higher his temperature, the graver was his condition. On the 8th, 9th and 10th days of hospital residence, he remained afebrile and showed gradual improvement. From the 12th to 19th days, the fever reappeared, probably owing to further dissection of the aneurysm, and the prognosis became more guarded.

The hypertension present on admission persisted for 2 days. On March 13, the blood pressure reading was within normal limits, 160/84. On March 14, there was a sudden rise of the temperature to 101°F, with extreme back pain and a concomitant fall in the blood pressure to 90/60 as the patient again sank into a state of shock. It was believed that the aneurysm had dissected and torn its way through the aortic hiatus of the diaphragm, because the pain in the region of the mid back was excruciating. The patient rallied following the administration of stimulants, and the next day presented marked icterus of the skin and sclerae.

On March 12, marked dullness on percussion was elicited in the interscapular area on both sides of the spine. Over this region one could hear a faint, low pitched and continuous roar that was not associated with or affected by the respiratory sounds over the lung hili. Over the course of days, the dullness gradually increased in extent and the bruit in intensity, until both could be heard distinctly from the pulmonary apices to the sacrum over the paravertebral regions. No visible or palpable pulsations were noted posteriorly at any time, and the patient was too sick to be fluoroscoped during his entire illness.

Auricular fibrillation set in on March 13, but responded promptly in rapid digitalization. The normal rhythm was occasionally interrupted by showers of extrasystoles, although the digitalis was reduced to a maintenance dose of 1½ gr daily beginning March 15. Accentuation of the second pulmonic sound became marked, and reduplication of the first sound appeared over both the aortic and pulmonic areas. This gave way to a systolic murmur over the mitral, aortic and pulmonary valves. On March 20, a tender pulsating mass appeared in the right lower quadrant of the abdomen. Duroziez's sign was prominent over this pulsating tumor, which disappeared 2 days later. The left border of cardiac dullness on percussion was found to be in the 6th interspace, 135 cm from the mid line. The cardiac sounds finally became loud and booming and could be heard readily throughout the entire chest and abdomen, both anteriorly and posteriorly. The head and neck were seen to jerk and throb with each systole. On March 29, the day before death, a large, tender, pulsating mass appeared in the left upper quadrant, rapidly filled this area and ballooned outward to the level of the umbilicus. A loud bruit was present over this tumor, which was thought to be a portion or a knob of the aneurysm, since no splenic notch could be felt and the blood picture remained essentially normal.

Probably the most interesting finding on physical examination was the discrepancy in the blood pressures in the two lower extremities. On March 15, a second electrocardiogram revealed inversion of T<sub>2</sub>, with T<sub>4</sub> biphasic. On this same day it was noted that the pulsation of the dorsalis pedis artery was more pronounced in the left foot than in the right. Unfortunately, comparative blood pressure determinations in the legs were not made until 3 days later, when the reading in the left leg was 249/106 and in the right leg 156/104. This discrepancy was still present on March 22, when readings of 244/105 and 140/98 were obtained in the left and right legs respectively. On March 25, identical readings (182/90) were found in each extremity.

Two days later, the patient's general condition seemed quite encouraging, and it was hoped that his improvement might continue. Since the pulsating mass in the right lower quadrant was no longer present and since the blood pressure readings had become equalized of their own accord, it was hoped that the periaortic aneurysm had dissected back into the main aortic channel just above the level of the iliac bifurcation, forming the so-called "double barrelled aorta." If this surmise had been correct, it was thought that a fatal outcome might be postponed for a considerable length of time.

On March 26 and 29, however, diarrhea and gaseous distention became increasingly distressing. A large, tender, pulsating mass appeared in the left upper quadrant, rapidly filling the epigastrium and extending down to the level of the umbilicus. There was no change in the blood pressure or in the blood picture, but the temperature rose to 101°F. It was believed that this condition was due to further dissection of the aneurysm below the diaphragm, the prognosis therefore became very uncertain.

Early on the morning of March 30, the patient experienced mild precordial pain, which was relieved by amnophylline. At 8:00 a.m., he stated that he felt fine and had no pain. Forty minutes later, he suddenly went into shock, and died while lying quietly in bed. The respirations persisted spasmodically for at least 3 minutes after the heart ceased beating. The picture during the agonal stage was one of exsanguination.

The final clinical diagnosis was dissecting aneurysm of the aorta, with death due to rupture of the aneurysm and massive internal hemorrhage.

**Autopsy.** Post mortem examination, performed 8 hours after death by Drs. R. E. Miller and W. M. Downing, of Hanover, New Hampshire, showed an extensive retroperitoneal hemorrhage to the left of the mid line from the splenic flexure of the colon down to the perirenal region and into the left portion of the pelvis. The peritoneum in these areas was dark red and purple owing to the underlying blood, but there was no evidence of intraperitoneal hemorrhage.

The right pleural cavity was dry, smooth and glistening. In the left pleural cavity, approximately 3 liters of hemorrhagic material, with massive blood clots in the dependent portion, was present. At the junction of the arch of the aorta with its ascending portion, an orifice 0.5 cm in diameter was encountered, which communicated with the left pleural cavity. This was the point of rupture of the dissecting aneurysm. The pericardium was not involved, and the heart itself appeared essentially normal with the exception of sclerosis of the aortic valve (Grade II), and extensive sclerosis of the root of the aorta and of the coronary arteries (Grade III). The peritoneal tissue in the lumbar regions and the perirenal fat on the left side were found to be heavily infiltrated with hemorrhagic material. At the point where the left subclavian artery arose from the arch of the aorta, there was a break in the intima of the aorta forming an orifice 0.3 cm in diameter that communicated with a space in the peritoneal adventitia extending from the region of the left subclavian artery down to the point of bifurcation of the common iliac vessels (Fig. 2). This peritoneal space did not completely surround the aorta at any point, but was filled with clotted blood. Five centimeters distal to the intimal rupture marking the origin of the dissecting aneurysm was located the point of rupture of the aneurysmal sac into the left pleural cavity. The peritoneal clot surrounding the right common iliac artery was so large that the true lumen of the vessel was markedly narrowed.

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ned. Although their cases were not typed, rains subjected to serologic classification all their into Group 1 or into what they called 1-3. The serums included both concentrated and unconcentrated lots, but all of them had high titers of antibodies (by the various criteria used) against the particular type occurred in this series. They also used larger of serum, and this may have been an important factor in the low mortality.

determining the value of antimeningococcus serum, one is thus left with a peculiar impression similar to that following the early use of pneumococcus serums, namely, that one is dealing with an agent that is apparently effective, conclusive proof of its effectiveness is lacking.

Of those who used the serums noted the clinical improvement in the patients who died; the best results occurred in the cases died early and in the young patients, except in the cases. Nevertheless, considerable conflicting concerning mortality in different communities, and at different times in the same community, leave an element of doubt concerning the relation the drop in mortality ascribed to the use of serum actually has had to the variations in disease at a particular time and place. The use of antimeningococcus serums is already involved in many of the same problems that later concerned workers concerned with the treatment of pneumonia: type variations, differences in mortality among the types and in different age groups, variations in the potency of serums and difficulty in estimating such potency by laboratory tests, the results of which have any correlation with clinical efficiency.

#### ANTERIOR POLIOMYELITIS

The problem of evaluating the use of convalescent serum in the treatment of anterior poliomyelitis presents an even more complex situation. In the first place, there is involved a serum that experimentally has been shown to have only what has been called "neutralizing antibodies."<sup>16</sup> There is no evidence that convalescent serums or antisera prepared against the virus in experimental animals are of any value in curing disease or in preventing paralysis even in animals, once the infection has taken hold. It is obvious that human beings cannot be treated at the same time that the virus is introduced. Therefore, theoretically, convalescent serum has no standing as a therapeutic agent, even on an experimental basis. Nevertheless, it has been accepted widely. It was only after experiments had been made to reinvestigate the problem by carefully controlling the results that any

element of doubt concerning the value of the serum was introduced.

In this disease, the mortality has shown wide variations in different epidemics, and even within the same epidemic in different communities. Similar variations in extent and severity of the paralysis have occurred during the same epidemic. Comparisons between cases that were serum treated and those that were not have been most difficult. One is dealing with a therapeutic agent accepted more or less on faith and used because in this disease no other effective therapy is available. The results, as reported, have been accepted without criticism. In 1932, Kramer and his associates<sup>17</sup> presented the results of their experiments in Brooklyn, and Park,<sup>18</sup> at the Association of American Physicians, presented the results of a large experiment undertaken jointly by the New York City Department of Health and the New York Academy of Medicine. These studies indicated that in two large contemporary series of cases the mortality and the extent of paralysis were almost identical, and, in fact, that the differences observed were slightly unfavorable for the serum-treated cases. The results were disbelieved by some workers and merely ignored by others,\* but they have since been confirmed.<sup>19</sup>

#### PNEUMOCOCCAL PNEUMONIA

Before turning to the immediate problem concerning pneumonia, one should consider some of the factors that are involved in determining the therapeutic efficacy of an antiserum for human patients after its beneficial effects in experimental animals have been clearly demonstrated. The chief factors may be listed as follows: the problem of diagnosis, including both the clinical and the etiologic diagnosis; the factors in the parasite or the invader; the factors in the host; the factors concerning the antiserum; the extent to which the host and the invader have interacted at the time when the antibody is administered; and the complications of the infection.

In diphtheria, the diagnostic problems are not very difficult. Treatment usually can be administered on the basis of clinical diagnosis, and the etiologic diagnosis is not too difficult to establish or to verify. The host is usually a young person, and complicating conditions in the host are not important factors. In infants, the prognosis is poor, as in most other severe infectious, and

\*Here again, one observes the mixed motives that sometimes confront the laboratory scientist when he is concerned with clinical experimentation. In discussing Park's paper, Flexner<sup>19</sup> stated "There is a consensus . . . that the use of convalescent serum does no harm. Since it cannot be affirmed that in an individual case it does no good, should its use be withheld? This is a question to be answered not by a pathologist but by a practitioner." Many a budding clinician hoping to bring a strict "scientific attitude" to bear on some of his bedside problems felt a bit disturbed by these remarks.

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## MEDICAL PROGRESS

### CONTROLLING CLINICAL THERAPEUTIC EXPERIMENTS WITH SPECIFIC SERUMS\*

With Particular Reference to Antipneumococcus Serums

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THE title of this paper might lead the reader to expect a scholarly dissertation including a historical review of attempts to control therapeutic experiments with biologic agents in human beings. Actually, it is the main purpose of this review to recount in an informal but critical manner some ten years of personal experience with attempts to determine the actual value of antipneumococcus serums in the treatment of pneumonia. Earlier data bearing directly on this problem were not very extensive and were quite inconclusive. Even when one turned away from pneumonia to other infectious diseases in which serums had been used, one could gain little either from the evaluation of the methods used or from the results obtained. At that time, there were at least three important diseases for which specific serums were available and had been used on a large scale with some attempt to control the results.

#### DIPHTHERIA

Perhaps the most successful therapeutic serum, and the one that has become definitely established as effective, is diphtheria antitoxin. This agent was introduced in 1890 by Behring, and was first widely used in human beings following the preparation of antitoxin in horses by Roux and Martin in 1894. It has been used in England and in the United States since 1895, and one of the first places where it was introduced successfully in this country was at the South Department of the Boston City Hospital. There is little question of the efficacy of antitoxin in neutralizing the lethal toxin of the diphtheria bacillus in animals. Efficient methods of preparing and titrating this antitoxin soon became available, and refinements of these methods were made as time went on. When one reviews the available data in an attempt to determine whether the use of this agent is actually effective in reducing the mortality from diphtheria, one is confronted with "a great body

of evidence that can be adduced in favor of the treatment . . . much of which can be interpreted in other ways."<sup>1</sup> For example, from previous experience, there is reason to believe that the severity of the disease is cyclic. Much has been acquired in the form of education in the recognition and early treatment of the disease. Hospitalization is more frequent, with accompanying improvement in general care. There have been improvements in general hygiene and diet that have perhaps increased individual resistance to infections. Much has been learned concerning the care of the patient with laryngeal diphtheria in the way of intubation, and reduction in mortality from tracheotomies probably resulted. The relative significance of these factors in reducing the mortality from diphtheria is hard to evaluate.

In 1923, Andrewes,<sup>1</sup> in a review for the Medical Research Council in England, summarized the evidence up to that time in two categories, one of which he termed "evidence of first rate value" and the other "evidence of secondary value." Some of the data in these categories are worth considering.

Unfortunately, only two therapeutic experiments could be classified as evidence of first rate value. One was that of Fibiger,<sup>2</sup> in Copenhagen, the report of which was published in 1898. This worker treated all cases admitted to the diphtheria wards on one day with serum, and those admitted on alternate days were treated without serum. There were, of course, some cases in which the diagnosis was never definitely established. If these cases are excluded, there were 239 cases treated with antitoxin, with 8 deaths, or a 3.3 per cent mortality, as compared with 245 patients treated without antitoxin, among whom there were 30 deaths, or a mortality of 12.2 per cent. There can be little criticism of this type of alternation of cases, since it is extremely unlikely that on the 'treated' days one would have a group of severe cases and on the 'untreated' days a milder group, or that any other factors might enter into consideration that would detract from the value of the data presented. The total number of cases was rather small. I hesitate in this discussion to

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proper controls. In Flexner's accumulated data, there was a mortality of 31 per cent after the exclusion of all cases in which deaths occurred within twenty-four hours, all chronic cases and all patients who were moribund when first treated or in whom there were mixed or intercurrent infections. This figure was compared with the mortality in untreated cases, from which no exclusions were made and which varied from 42 to 80 per cent, averaging 70 per cent. In the treated cases, the efficacy of therapy was shown to vary with the time at which it was administered. It was most effective if given within the first three days of the disease. Cases treated during this time had a mortality of 18 per cent, those treated from the fourth to the seventh day had a mortality of 27 per cent, and those treated after the seventh day, 37 per cent. Flexner also showed a relation to age, with the highest mortality in the group under one year of age and the lowest mortality in the group between five and ten years. Clinically, the most rapid recovery occurred in the favorable age group, and there were fewer complications among the treated cases.

Dopter<sup>12</sup> summarized the French cases treated with serum from the Pasteur Institute. In his series, there was a mortality of 14.5 per cent before exclusion of the moribund cases and those complicated with other infections, and 11.7 per cent after such cases were excluded. In cases treated without serum, the mortality during the same period was 65 per cent.

Experiences with antimeningococcus serums first brought out the importance of type specificity. Specific types of meningococcus were recognized and classified in 1909 more or less simultaneously by three different workers. Hine,<sup>13</sup> in reviewing the results of serotherapy in some of the British forces during World War I, showed that the treatment was highly effective in Type 1 and Type 3 cases, and was much less satisfactory in Type 2 cases, but the number of cases was small. In his first series, there were 90 cases, 34 of which were Type 1, with 1 fatality; 10 were Type 3, and all these patients survived; and there were 7 deaths among 32 Type 2 cases. He emphasized the value of early treatment, daily doses, prompt typing, adequate use of the appropriate serum and the administration of large doses for Type 2 cases. These arguments have become commonplace, since the various therapeutic experiments with antipneumococcus serums emphasized the significance of each of these points. In a second series, including moribund patients but excluding those with intercurrent diseases, there were 141 cases, with 19 per cent deaths among those treated within

the first six days. There were 65 cases with 9 per cent deaths among patients with Type 1 infections, 39 per cent among 104 with Type 2, and 25 per cent among 28 with Type 3. Unfortunately, an epidemic of influenza intervened at the time of the second series, so that part of the mortality may have been due to that cause. There were 48 untyped cases in this series, with a mortality of 45 per cent.

Numerous reports concerning the use of antimeningococcus serum have appeared since the early studies of Flexner and Dopfer. Not all have been quite so favorable. One carefully controlled study carried out in Detroit by Gordon<sup>14</sup> shows how any one group of figures collected over a limited period might be misleading. In his report before the Association for Research in Nervous and Mental Diseases in 1931, Gordon tabulated the mortality from meningococcal meningitis in the Detroit area and from the Herman Kiefer Hospital for the years 1922 to 1931. All the cases during this period were treated with serum. The mortality in the endemic years 1922 and 1923 was 65 and 55 per cent, respectively. In the pre-epidemic years 1924, 1925 and 1926, the mortality was 19, 14 and 41 per cent, respectively. In 1927, there began an epidemic that reached its peak in 1929 and subsided in 1931. During this period, the mortality rose sharply to a peak of 65 per cent, and then dropped to 42 per cent. For the most part, only one type (Type 3) was found to be the causative agent. The serum at first was polyvalent with a low titer for Type 3, but was later monovalent and of high titer. The results indicate clearly either that the efficacy of antimeningococcus serum was misjudged or that other factors were introduced which militated against the best results. One point might be mentioned that has been illustrated in the low figures of 19 and 14 per cent, which Gordon reported for the endemic years 1924 and 1925, namely, in some endemic periods the mortality may be low, or during such periods good serums may be available against the particular strain that causes the infection. This feature is also brought out in the striking results that Tillett and Brown<sup>15</sup> reported from Johns Hopkins Hospital during the spring of 1935, when they had only 1 death among 25 consecutive treated cases.

Tillett and Brown's results, although not conclusive, may hold the answer to another secret concerning mortality, which has been perhaps more clearly revealed in the use of antipneumococcus serums. They employed serums prepared in the New York State Laboratory. These serums were of uniform quality and of high potency against the particular type with which they were

concerned. Although their cases were not typed, the strains subjected to serologic classification all fell either into Group 1 or into what they called Group 1-3. The serums included both concentrated and unconcentrated lots, but all of them contained high titers of antibodies (by the various laboratory criteria used) against the particular type that occurred in this series. They also used larger doses of serum, and this may have been an important factor in the low mortality.

In determining the value of antimeningococcus serum, one is thus left with a peculiar impression similar to that following the early use of antipneumococcus serums, namely, that one is dealing with an agent that is apparently effective, but conclusive proof of its effectiveness is lacking. Most of those who used the serums noted the rapid clinical improvement in the patients who responded; the best results occurred in the cases treated early and in the young patients, except infants. Nevertheless, considerable conflicting data concerning mortality in different communities, and at different times in the same community, leave an element of doubt concerning what relation the drop in mortality ascribed to the use of serum actually has had to the variations in the disease at a particular time and place. The use of antimeningococcus serums is already involved by many of the same problems that later confronted workers concerned with the treatment of pneumonia: type variations, differences in mortality among the types and in different age groups, variations in the potency of serums and difficulty in estimating such potency by laboratory tests, the results of which have any correlation with clinical efficiency.

#### ANTERIOR POLIOMYELITIS

The problem of evaluating the use of convalescent serum in the treatment of anterior poliomyelitis presents an even more complex situation. In the first place, there is involved a serum that experimentally has been shown to have only what have been called "neutralizing antibodies."<sup>16</sup> There is no evidence that convalescent serums or antisera prepared against the virus in experimental animals are of any value in curing disease or in preventing paralysis even in animals, once the infection has taken hold. It is obvious that human beings cannot be treated at the same time that the virus is introduced. Therefore, theoretically, convalescent serum has no standing as a therapeutic agent, even on an experimental basis. Nevertheless, it has been accepted widely. It was only after attempts had been made to reinvestigate the problem by carefully controlling the results that any

element of doubt concerning the value of the serum was introduced.

In this disease, the mortality has shown wide variations in different epidemics, and even within the same epidemic in different communities. Similar variations in extent and severity of the paralysis have occurred during the same epidemic. Comparisons between cases that were serum treated and those that were not have been most difficult. One is dealing with a therapeutic agent accepted more or less on faith and used because in this disease no other effective therapy is available. The results, as reported, have been accepted without criticism. In 1932, Kramer and his associates<sup>17</sup> presented the results of their experiments in Brooklyn, and Park,<sup>18</sup> at the Association of American Physicians, presented the results of a large experiment undertaken jointly by the New York City Department of Health and the New York Academy of Medicine. These studies indicated that in two large contemporary series of cases the mortality and the extent of paralysis were almost identical, and, in fact, that the differences observed were slightly unfavorable for the serum-treated cases. The results were disbelieved by some workers and merely ignored by others,\* but they have since been confirmed.<sup>19</sup>

#### PNEUMOCOCCAL PNEUMONIA

Before turning to the immediate problem concerning pneumonia, one should consider some of the factors that are involved in determining the therapeutic efficacy of an antiserum for human patients after its beneficial effects in experimental animals have been clearly demonstrated. The chief factors may be listed as follows: the problem of diagnosis, including both the clinical and the etiologic diagnosis; the factors in the parasite or the invader; the factors in the host; the factors concerning the antiserum; the extent to which the host and the invader have interacted at the time when the antibody is administered; and the complications of the infection.

In diphtheria, the diagnostic problems are not very difficult. Treatment usually can be administered on the basis of clinical diagnosis, and the etiologic diagnosis is not too difficult to establish or to verify. The host is usually a young person, and complicating conditions in the host are not important factors. In infants, the prognosis is poor, as in most other severe infections, and

\*Here again, one observes the mixed motives that sometimes confront the laboratory scientist when he is concerned with clinical experimentation. In discussing Park's paper, Flexner<sup>19</sup> stated "There is a consensus . . . that the use of convalescent serum does no harm. Since it cannot be affirmed that in an individual case it does no good, should its use be withheld? This is a question to be answered not by a pathologist but by a practitioner." Many a budding clinician hoping to bring a strict "scientific attitude" to bear on some of his bedside problems felt a bit dismayed by these remarks.

specific serum therapy is least effective. The infecting organism in diphtheria was formerly thought to be uniform in its virulence and toxin production, but it is now recognized that both these factors may vary, as already noted. This factor is the most significant in considering the value of previous reports on this disease. Standardization of the antibody has been fairly well established. Antitoxin is comparatively uniform in quality, at least within the range necessary for therapy. Even on this point, however, there is now some doubt, since the relation between the antibodies produced by toxin from the various types of diphtheria bacilli cannot be evaluated properly at the moment. It is recognized in diphtheria, as in other diseases, that the earlier the treatment is undertaken the better the results. This is corroborated by fairly reliable data. Most reports that deal with numbers large enough to be of value, however, indicate that antitoxin has a definite effect at any stage of the disease. The reason why the results of the therapy of diphtheria in certain recent epidemics have been less favorable than in the past is now ascribed to the occurrence of the gravis organisms. The effectiveness of antitoxin against infections with this type will have to be re-evaluated. Complications of the infection itself are related directly to the action of the toxin, or to mechanical complications in laryngeal involvement. The incidence of laryngeal diphtheria and the methods by which this form of the disease is handled, aside from the specific antitoxin, are also major factors in the fatality rates in the serum-treated cases.

The diagnosis of meningitis is usually not difficult, especially in epidemics. The host factors are not much more disturbing in this disease than in diphtheria. The problems concerning the invader are important, since the mortality from different types varies considerably, and since the efficacy of the serums against each type is apparently also quite variable, being most effective against the Type 1 and least effective against the Type 2. The antibody presents difficulties in standardization that have not yet been entirely overcome. The use of in vitro tests, such as the agglutination, complement-fixation and precipitation tests, has not always paralleled the results of protection tests, which are difficult to standardize. The stage of the disease when treatment is begun presents the same problem as that of diphtheria. The complicating factors in the treatment of meningitis are such as may interfere with the efficiency of treatment; for example, the development of spinal-fluid block or the deposit of thick layers of fibrin that enclose collections of purulent material not amenable to drainage. These

complications may maintain the organisms locally after the general infection has been overcome.

In poliomyelitis, the diagnostic problems are difficult to evaluate, particularly since they have been complicated with the question of so called "paralytic poliomyelitis." The etiologic diagnoses are made essentially on clinical grounds and cannot at present be established. The hosts are usually young. The problem of variations in virulence of the invader is recognized but not understood. The serums are practically impossible to standardize at the present time, so that the entire choice of specific therapy in poliomyelitis rests on rather precarious grounds, as demonstrated in the most recent therapeutic experiments.

At the time when the attempts to evaluate serum therapy in pneumonia were first made in a serious manner at the Boston City Hospital,<sup>29</sup> there were difficulties on all scores. Some of these problems have since been solved, but most of them still remain. Since treatment was then limited to cases of typical lobar pneumonia, the clinical diagnosis was relatively simple. Etiologic diagnosis was complicated by the fact that treatment required type-specific antibody, at least so far as could be ascertained from animal experiments. Type diagnosis was then still a time-consuming matter. There was, in addition, the difficulty of determining the etiologic relation to the disease of any pneumococcus type found in the sputum, since that was the main source of material for typing. The occurrence of bacteremia in any given case usually solved the problem of the etiology for the particular patient concerned. Even this fact, however, frequently became known only some time after a type diagnosis had been made from the sputum. There was also the factor of mixed infections, since it is rare to obtain pure cultures of pneumococci from sputum, particularly in the early stages of the disease when serum might be expected to be most effective. Host factors in pneumonia were obviously of the greatest consequence, particularly in large municipal hospitals, where a great number of the patients are in old age groups and suffer from degenerative diseases. Many of the patients of all ages may be affected to some degree by nutritional disturbances, and a great many adults suffer from chronic alcoholism. With respect to the parasite, there was of course the problem of specific types of pneumococci already mentioned. In addition, the possibility that the virulence might vary from year to year, even with the same type, was a factor. The extent to which the host and the invader have interacted at the time that specific treatment is begun is, of course, most significant



1 cases of pneumonia. This became clear from the very start when the attempt was made to treat patients regardless of how long they had been sick.<sup>20</sup>

The antibody itself presented more than its share of difficulties. Part of the problem later on concerned the evaluation of the toxicity of various lots of serum. It was soon recognized that serum reactions were entirely independent of antibody content and interfered considerably with the therapeutic end results. In fact, these untoward reactions often made it impossible to use some lots of serum. The methods of refining and concentrating antibody were being developed at the same time, and considerable controversy was aroused among some workers about the relative antibody content and therapeutic value of concentrated and unconcentrated serums. The controversy hinged on the procedures used in evaluating potency, which until recently depended solely on the mouse-protection test.

Complications from pneumonia may, of course, in themselves be fatal, even after the acute disease in the lung has subsided. They are recognized as occurring in the severest cases and in those in which invasion of the blood stream has occurred, but they usually appear late in the disease. Thus, the question of delayed therapy is intimately related to that of complications.

All the early studies were carried out with horse serums. Antibodies of high titer were attained in horses with great regularity against Type 1 pneumococci, but Type 2 antibodies were difficult to produce in high titer, and different horses varied considerably in this respect. The Type 3 pneumococcus presented a hopeless problem, since significant amounts of antibody for this type could not be produced. After the newer classification of pneumococci became established, it was recognized that some of the new types, which were most prevalent, were highly antigenic in horses, and good titers against them were regularly obtained. Notable among these was Type 5. More recently, it has become possible to produce in rabbits highly potent therapeutic serums against all types of pneumococci.

At the Boston City Hospital, there had been two clinical experiments in the serum therapy of pneumonia before Sutliff and I began our studies. The first was that of Locke and the workers on the Pneumonia Service, which was organized during the great influenza epidemic and continued through the year 1922. Locke<sup>20</sup> attempted to carry out a very carefully controlled study with the Type 1 serum prepared in the Massa-

chusetts Antitoxin and Vaccine Laboratory according to the methods developed at the Rockefeller Institute. The results at the Rockefeller Institute, as well as those in other clinics, were not very convincing. There were no controls. Locke, during the first year of his study, treated all Type 1 cases, and during the subsequent two years treated a strictly alternated series of Type 1 cases. The final result in groups of about 70 cases each showed an almost identical mortality in the first year, when all Type 1 cases were treated, and in the second year, both in the treated cases and in the alternate control cases. The only indication that there might be some curative value in the serum that he employed appeared from the results of the 12 treated cases in which the serum was given before the end of the third day of illness. None of these patients died. Locke was dealing with unconcentrated serums, whose potency may have been extremely low, as later shown by Felton and Stahl<sup>21</sup> in their survey of the problems of standardization.

It is interesting that the mortality from Type 1 pneumonia in each of Locke's three series was about 17 per cent. A more careful survey of these cases shows that during the first period there was but a 17 per cent incidence of bacteremia, and that during the second period, the treated cases had a bacteremic incidence of 44 per cent, as compared with 22 per cent among the controls. All the studies in both treated and untreated cases during the last ten years have indicated that the mortality is directly proportional to the bacteremic incidence. In untreated cases, except in those due to Type 3 pneumococcus, which are almost invariably fatal if the blood is invaded, the bacteremic incidence practically tells the mortality in any group of cases.<sup>22</sup>

Following Locke's study and beginning in the year 1924, the Department of Preventive Medicine and Hygiene of the Harvard Medical School became interested in a therapeutic experiment at the Boston City Hospital. In this study, alternate cases were treated with various lots of serum, which Felton had prepared by various methods of concentration. The study was conducted by a single resident, who was under the general direction of Felton, and had the clinical supervision of Locke and Robey. This resident obtained sputum for typing and treated alternate cases that were called to his attention in which a definite clinical diagnosis of pneumonia was made. The records of both treated and control cases were turned in to Felton. There was a different resident each year, and when I undertook the studies there had been five years of this experiment. From

the records available for these years, an attempt was made to analyze the results of the serum therapy. Utilizing the experience of Locke and also considering that the experiment was done with bivalent serum containing Type 1 and Type 2 antibody, we attempted to learn: whether the serum therapy produced a reduction in mortality; whether the reduction was greater in the cases due to Types 1 and 2 pneumococci than in the others; and whether the patients treated early in the disease were benefited more than those treated late. It was also of interest to learn whether this rather impersonal method of handling a therapeutic experiment resulted in reliable and comparable groups of treated and controlled cases.

The mortality figures<sup>23</sup> showed that the cases of Type 1 and Type 2 pneumonia treated within the first three days of the disease had a definitely lower mortality than the untreated cases, or than the cases treated on the fourth day or later. The disturbing feature was an apparent reduction in total mortality in the Type 3 and so-called "Group 4" cases. These patients had received the bivalent (Types 1 and 2) serums, which contained no specific antibody for the types with which they were presumably infected.

It was assumed that the successive residents treated alternate cases as long as they had serum, discontinued their experiments when no serum was available, and kept records only during the time that the experiment was going on. It was of some interest, therefore, to find out to what extent two important factors might have influenced the choice of cases: one was the stage of the disease, and the other was the age. In other words, it was essential to determine whether a larger proportion of the younger patients and more of the patients admitted early in the disease might have been treated with serum to account for the differences in mortality in the serum-treated Types 3 and 4 cases. It has been well recognized that mortality in pneumonia, regardless of the etiologic agent, increases with advancing age. If a larger number of old people were included in any groups, obviously the gross mortality figures would be influenced unfavorably. On analyzing the data on this point, it was easily shown that the so-called "control cases" had a definitely unfavorable age distribution. This was also true of the distribution according to the stage of the disease. Among the serum-treated cases, a larger percentage were admitted early in the disease, and fewer late cases were included. To offset this factor and at the same time to obtain some idea of the effect of serum on the course of the disease, it was necessary to compare the total duration of the acute disease in

the Type 1 and Type 2 treated cases with that of similar patients who were not treated with serum and who were admitted to the hospital at the same stage of the disease. This was done by comparing the average total duration of the acute disease (using arbitrary but similar criteria) with the duration of the illness at the time of admission to the hospital. In this way, it was shown that the duration of acute illness was shortened in Types 1 and 2 cases by early serum treatment. Also, among the Type 1 cases, composite temperature charts were constructed for the patients who recovered without complications, one for those treated with serum, and another for those who were not treated with serum. When these composite temperature charts were constructed so that they began with the first day in the hospital, differences between the treated and the untreated groups were not apparent. However, a rearrangement of the data according to the day of onset of the disease showed a definite reduction in the total period of febrile illness among the Type 1 treated patients who recovered.<sup>23</sup>

When, in 1929, Sutliff and I attempted to formulate further plans for the evaluation of serum therapy, it became obvious that it would not be possible, within a period short of several years, to produce reliable and significant evidence on the basis of mortality figures. We therefore attempted to use the results in individual cases as a basis for comparison, following treated and untreated cases very carefully and alternating serum therapy by a strict method, which was controlled entirely in the laboratory. Serum was given to alternate cases of each type as soon as the type was determined. From the very start it became obvious that such controls were only self-deluding. We were confronted with patients in whom the type was determined after the patient was already dead, and others who were moribund when the results of the typing became known. We soon limited our experiments to those patients who, at the time the type was determined, were ill for four days or less. This, in addition to the fact that an ample supply of highly potent Type 2 antibody was available, made it possible to include both Type 1 and Type 2 cases in such an experiment.

The results from the point of view of mortality are difficult to evaluate because the numbers were small. The clinical effects of serum were determined by using the temperature and general symptoms as criteria. The results in Type 1 cases during the first year were thus tabulated. By all recognized criteria for clinical recovery, the termination of the disease in serum-treated cases was shown to be in relation to the time when the

type was determined, and thus to the time when the serum treatment was given. This was demonstrated clearly in this first year's experience, in which all Type 1 cases were included, regardless of the time of admission.<sup>24</sup> Similar results were demonstrated, even more clearly in the cases of Type 1 pneumonia, both treated and untreated, during the next three years.<sup>25</sup> The duration of acute symptoms was always relatively short in treated cases, and comparatively long in untreated cases. Symptoms of the acute disease rarely persisted beyond the fourth day in the patients admitted early and treated with serum, and rarely ended before the fourth day in those who were not treated with specific serum. Similar results were also demonstrated in Type 2 cases.<sup>26</sup>

During the time when only Type 1 and Type 2 serums were available, we tried to obtain as many data as possible on all other cases of pneumonia, from both the clinical and etiologic points of view. We attempted to type all cases in which pneumonia was suspected, followed them, and eventually analyzed the results with the hope of having a background for comparison when new serums or other remedies became available. A survey of these cases, as well as of those that were treated, showed certain constant features with regard to mortality: bacteremic patients always had a much higher mortality than corresponding patients without bacteremia; the mortality increased with advancing age; in serum-treated cases, there was a general correlation between the time of treatment and mortality,—the earlier in the disease treatment was begun the lower was the death rate; the greater the extent of the pulmonary lesion at the time when the patient was admitted to the hospital or when treatment was begun, the higher was the mortality; the development of infected focal complications increased the death rate; the occurrence of underlying acute or chronic disease had a marked influence in increasing the death rate in both treated and untreated cases.

As time went on and better serums became available for Type 1 and Type 2 cases, as well as for other types, it became clear that we were concerned as much with the problem of the conditions under which these serums were useful in reducing mortality or in cutting short the disease as we were in the general reduction in death rate.

During the early experiments with the serum treatment of pneumonia, as already mentioned, alternate patients were given the bivalent serum before the type determination was made. At that time, one feature of the effects of serum treatment was more impressive than any other. When a

patient who had been ill for four days or less was admitted to the hospital and given serum, if he was well the next morning, the type was almost always found later to be either Type 1 or Type 2. This seemed to us at the time to be the best clinical evidence for the effectiveness and specificity of the serum, in spite of the fact that this was difficult to express in a convincing form, except by comparing the clinical course of the disease in treated and untreated cases in the manner already mentioned. However, when a larger body of data became available, which was sufficient to be analyzed into the factors that I have already outlined, the mortality figures also appeared to be significant and convincing. The available figures are illustrated in the reports<sup>27</sup> on the results of treatment in Types 1, 2, 5 and 7 cases during the nine-year period from 1929 to 1938.

The outstanding features of these mortality figures are: an increasing proportion of cases were submitted to serum therapy; a constantly low mortality was observed in those treated with serum; and a constantly high mortality was noted in patients who escaped serum therapy for one reason or another—many of the patients who escaped serum therapy in the latter years were diagnosed either after recovery or at autopsy.

In addition to the gross fatality rates, a large amount of clinical evidence based on the following facts has been gathered: there is a definite relation between treatment and recovery; bacteremia is arrested following serum therapy; the spread of the disease in the lung is arrested following serum administration; except in those treated very late in the disease, the mortality in serum-treated cases is always lower than in comparable cases not treated with serum—this is true in all age groups, in bacteremic and nonbacteremic cases, in those with limited or extensive lung involvement, and in those with and without complications or other predisposing conditions; and the beneficial results of serum therapy are strictly type specific.

Another important feature in the evaluation of the therapy has been the fact that in all but a very few cases, failures to obtain striking beneficial results following serum administration could be traced to certain well-defined causes. These are, briefly: delayed treatment; inadequate therapy or improper treatment in the sense of spreading dosage over a long period—the use of serums of low potency falls in this category; misdiagnosis, that is, etiologic misdiagnosis, which includes errors in typing and the improper evaluation of the relation of the bacteriologic finding to the etiology of the disease; the presence of focal

complications, notably empyema, at the time treatment is begun; and the pre-existence of severe systemic disease such as cardiac or renal failure, cerebrovascular accidents and alcoholic delirium. How or why these factors interfere with the results of therapy is not within the scope of this presentation. It is obvious that many of these conditions, which are unfavorable from the point of view of specific serum therapy, may nevertheless be influenced favorably by other types of treatment, as we have seen since the introduction of chemotherapy.

If an attempt is made to summarize our experience in pneumonia in relation to the experiences of others with various infectious diseases, we find that the actual attempts to demonstrate reductions in mortality by carefully controlled clinical experiments were not entirely successful and were essentially abandoned in favor of the careful observation of individual cases for the beneficial effects of serum or for the causes of the failure to obtain such beneficial effects. We were led to the belief that therapeutic antipneumococcus serum, if it were effective, should demonstrate its benefits in every case in which it is used unless definite and recognizable factors are present that militate against its efficacy.

In conclusion, it is probably safe to say that in the evaluation of treatment in a disease like pneumonia one must rely on the integrity of the reporter to present all the relevant facts. Only when all the details are presented is it possible to demonstrate the efficiency of the agent in question. The differences between treated and untreated cases must be unequivocal and must be consistent. Only in this manner can the reporter himself be really convinced of the significance of his results. The reader of his reports can become satisfied only when he goes through similar experiences and is likewise impressed with successive individual results.

The relation of serum therapy to chemotherapy is not strictly within the scope of this paper. However, since this is now the only problem of importance with respect to the use of serum in pneumonia, it will be considered briefly.

It is generally conceded that chemotherapy with one of the sulfonamide drugs, notably sulfapyridine or sulfathiazole, is now the treatment of choice in cases of pneumonia.\* The question arises whether the use of specific serum in addition to one of these effective sulfonamides is more beneficial than the treatment with that drug alone. From what has already been said concerning the evaluation of antipneumococcus serums, it is ob-

vious that this question is considerably more difficult to answer decisively on the basis of strictly controlled clinical studies.

Since adequate data have been brought forth to attest the efficacy of the sulfonamides, it is no longer possible to deny any patient with pneumonia the benefits of their use. Even a delay in the application of chemotherapy is justly open to criticism because with these drugs, as with other remedies, early treatment is essential for the best results. Furthermore, the ease of administering the drugs and the frequency and rapidity with which the pneumonias respond to their use make additional therapy useful, at best, only in selected cases that do not yield readily to the drugs alone. It is difficult to see how a clinical experiment that takes these factors into account can yield a decisive answer to the question at hand.

In the cases treated at the Boston City Hospital,<sup>29</sup> an attempt was made to compare the results of treatment with serum and sulfapyridine used separately and in combination, to determine the conditions under which each type of therapy might be most advantageous. The combined therapy was used in the severest cases, and in patients who did not seem to improve under treatment with one or the other agent when used separately. A large proportion of the cases in which the combination of serum and drug was used may, therefore, be classed as failures, or threatened failures, from chemotherapy. Similar data have been reported from most of the other clinics in which such studies have been undertaken. Obviously, no conclusions can be drawn from such data concerning the relative merits of the drug alone and of the combined therapy. Our results suggest that in most of the cases with the worst prognosis, the use of serum in addition to sulfapyridine may increase the chances of recovery and may shorten the duration of the acute illness in patients who survive. The results in individual cases, although they generally support this view, still leave room for doubts.<sup>30</sup>

In two recent reports, the attempt has been made to cope with this problem by setting up strict criteria for the choice and alternation of cases. Dowling, Abernethy and Hartman<sup>31</sup> alternated their cases within each type of pneumococcus as soon as the type was determined, one case being given sulfapyridine alone and the next receiving both this drug and serum. To avoid too great a delay in initiating therapy, every patient in whom the pneumococcal type was not obtained within six hours was excluded from the study and given sulfapyridine. In the patients who received the combined therapy, recovery was more rapid than in

\*The relevant literature on this subject has recently been summarized.<sup>32</sup>

ose treated with the drug alone, as judged by average duration of fever. In the patients over 40 years of age, the mortality was also lower with the combined treatment. The only serious objection to this study is the small number of cases involved.

In the second report, by Plummer and his associates,<sup>3</sup> all patients were treated with some sulfonamide drug as soon as the clinical diagnosis was made, and alternate cases within each type were placed in the series treated by serum in addition to the drug. Some of the patients were already dead and others were afebrile at the time the type was determined; they received no serum, but were nevertheless retained in the group receiving combined treatment. From a comparison of the death rates and of composite temperature curves, these authors concluded that there was no significant difference in the results of treatment in the two series.

It is rather odd, in view of the strict alternation of types stressed by these authors, that for many of the types there is a preponderance of cases either in the series treated with the drug alone or in the combined therapy series. The length of the delay before serum treatment was given in most cases is not mentioned, but in some of the cases it was as long as twenty-four hours. Furthermore, although mention is made of the number of patients who received serum and died within twenty-four hours, the total number of patients who actually received serum is not given. Moreover, a considerable portion of the mortality among the patients who received combined treatment occurred within twenty-four hours of admission to the hospital, whereas only a small number of those receiving the drug alone died within twenty-four hours of entry. Although it is possible to deduce from these data that some of the fatalities were the result of the serum therapy, it seems much more probable that some unconscious selection on the part of the authors played an important role in the inclusion of the poorest subjects among the serum recipients. This is only a natural occurrence, since there is always a tendency to give to the patients who seem the most severely ill the benefits of any remedy that is known to be effective. It is likewise natural, particularly in view of the time and effort required for serum administration, to avoid giving this type of therapy to patients who seem to be improving adequately without it.

The conclusions drawn by these authors may or may not prove to be correct, but one cannot help believing that the results as presented are

not only inconclusive but even grossly misleading. It would likewise be erroneous to draw any conclusions regarding the relative merits of these two types of treatment from mortality figures obtained from reports in which the selection of cases was not strictly controlled. This is true of groups of cases from a single clinic, such as those I have presented,<sup>29</sup> but it is all the more true of cases gathered by central agencies from the reports of scattered physicians.

The two studies that have been discussed concerned adults. Another controlled study, carried out in infants and children, was reported by Carey.<sup>33</sup> He alternated his cases as soon as the diagnosis of pneumonia was made and the pneumococcus typing was completed. In cases in which the causative organism was found to be a pneumococcus for which specific antipneumococcus serum was available, alternate patients who were not serum sensitive received serum in addition to the drug. This alternation was not followed strictly because of certain patients in whom either typing was delayed or a mixed infection was present, and it was not immediately clear which was the causative type. In such cases, chemotherapy was started, and the patients were frequently well when the question of serum therapy arose. The fatality rates in all groups of cases were so low that comparisons were not justified.

The average duration of the disease was compared and was of some interest. It was found that the duration in the treated cases was the same after sulfapyridine as it was after sulfathiazole. The outstanding finding in this series, however, was that the average duration of the pneumonia after treatment was appreciably shorter in those patients who received specific antipneumococcus serum in addition to sulfapyridine or sulfathiazole, as compared with the duration of the acute illness after treatment with sulfapyridine or sulfathiazole alone.

The question whether the use of serum in addition to a sulfonamide is superior to the use of the drugs alone thus remains unanswered. It is my opinion that this particular question as it concerns pneumonia is now a highly academic one, since it is unlikely that any physician would contemplate using the combined therapy as a routine in all cases. It seems far more important to concentrate on the failures of chemotherapy and attempt to determine, first, whether such failures can be predicted, and then which of them can be averted by the use of serum. Even this is not a simple task. Fortunately for the patient with pneumonia, however, the failures from chemiotherapy are few.

A reply by Dr. Plummer to the author is published in the issue of the Journal (page 51).

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CASE RECORDS OF THE  
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

## CASE 27391

## PRESENTATION OF CASE

A thirty-seven-year-old man entered the hospital complaining of fatigue, hemoptysis and pain in the left arm.

Two years before admission, the patient noticed that he was becoming unduly fatigued, and that rest gave him no relief. He carried on until eight months before admission, when a small hemoptysis—about one teaspoonful—occurred, without other symptoms referable to the respiratory system. A chest plate was taken immediately, and a diagnosis of tuberculosis of the left apex made; the patient was sent to a sanatorium, where intensive studies were carried out, including x-ray films, fluoroscopy, lipiodol injection, bronchoscopy, a punch biopsy of the lung and sputum examinations. The patient was told that tuberculosis was definitely ruled out and that the most likely diagnosis was a low-grade infection of the lung, possibly due to a fungus. With sanatorium care and potassium iodide treatment, he improved and was able to return to work at the end of four months.

Eight weeks before admission, fatigue returned, and a dull gnawing ache developed in the left anterior chest. In addition, along the inner surface of the left arm immediately below the axilla, he noticed pain that gradually spread down the lateral surface of the arm as far as the mid-forearm. Both pains increased in severity, the arm pain becoming the more pronounced of the two. Six weeks before admission marked the onset of night sweats, which were still a symptom at the time of admission. Two weeks before entry, the patient went to Florida, but after several days developed a fever rising to 102°F. He entered a hospital, and the fever subsided within a few days; x-ray films were taken, and he was referred to this hospital. There had been a loss of 10 pounds in weight in the previous eight months. Cough and sputum were never very marked symptoms, the latter being limited to a half teaspoonful a day, raised in the morning and perhaps once again during the day. It consisted of brown purulent material.

On examination, the patient was well developed and well nourished and not in apparent distress.

Examination of the heart was negative; the blood pressure was 130 systolic, 70 diastolic. In the upper left chest, from the supraclavicular fossa down to the third rib anteriorly and the fourth thoracic vertebra posteriorly, there was dullness to percussion, with diminished tactile fremitus and breath sounds, but no rales. The abdomen was normal except for a small right inguinal hernia.

The temperature was 99°F., the pulse 100, and the respirations 22.

Examination of the urine was negative. Examination of the blood showed a red-cell count of 4,330,000 with a hemoglobin of 13.6 gm. (photoelectric-cell technic), and a white-cell count of 8900 with 82 per cent polymorphonuclears. The nonprotein nitrogen of the blood serum was 28 mg. and the protein 6 to 7 gm. per 100 cc.; the blood Hinton reaction was negative. Repeated examinations of the sputum were negative for tubercle bacilli and actinomyces; cultures yielded rare colonies of beta hemolytic streptococci, with a predominance of alpha hemolytic streptococci.

An x-ray film of the chest showed an area of dullness occupying the upper portion of the left lung field. In films taken in the usual manner, the shadow appeared to be of homogeneous density and extended from the extreme apex to the third rib in front; the trachea and mediastinal contents were not displaced, and the diaphragm on this side was in the usual position and only slightly limited. The lung fields, except for the area described, were normal in appearance. The heart shadow was not increased in size or abnormal in shape, and there was no displacement. In a film taken with the Bucky diaphragm, the lower half of the shadow presented a mottled appearance, with dense lines running through it suggesting the walls of bronchi or trabeculation. The margins of the shadow were quite dense, and the lower border was convex. In the lateral view, the shadow appeared to extend from the anterior to the posterior wall, and its greatest extent was in the middle part of the chest. The trachea appeared to lie anterior to it; there was no visible pulsation.

A review of films taken in other hospitals showed that a little over two years before admission, the left apex was clear and there was no visible tumor mass. There was, however, some increased radiance in this portion of the lung, suggesting air trapping. Seven months before admission, the mass was about half its size on entry and had a similar structure and appearance. In films taken with the patient lying on his back, in other hospitals and here, a widening of the second interspace in the axillary line was evident.

There was no evidence of a destructive process in the ribs in any of the films, and no visible calcification within the mass.

Each day, the sputum was dark reddish brown, and the patient said it had been exactly similar for the past eight months. The pain in his arm grew worse, and was no longer controlled by aspirin and codeine. On the ninth hospital day, constriction of the left pupil was noticed for the first time. The next day, an operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR. THEODORE L. BADGER:<sup>\*</sup> May we see the x-ray films?

DR. AUBREY O. HAMPTON: This first examination was made in 1938, when the chest was considered normal. There might be the slightest variation in density between the lung apices, the left being thought by some observers to be a little more radiant than the right. This next film, which was taken two years and two months later, shows a fairly homogeneous dense shadow occupying the region of the left upper lobe, with perhaps a little mottling. There is no displacement of the trachea and no disease in the ribs. The remainder of the lung fields is clear. Still later films show little or no increase in the total size of the mass, but the mottling has become more prominent and there is a strong suggestion of cavitation. These are laminographic films, and this is the same area seen on the plain film. The inferior margin of the shadow is sharp, and within it there are mottled 1-cm. to 2-cm. areas of rarefaction, which are almost like a cluster of grapes, very regular in size. Another significant finding is an unusually straight bronchus, which looks as though it were being pulled on and runs into the area of disease. It filled irregularly with lipiodol. No lipiodol entered the area of disease, and the trachea and main bronchus were not pressed on. In summary, the film shows a fairly sharply defined shadow continuous with the ribs and the apex of the lung and, in the lower portion, multiple cavities of almost the same size. There is also a straight rather drawn-out looking irregular bronchus.

DR. BADGER: Summarizing briefly this complicated and rather difficult case, the outstanding features of the history are two years of fatigue, and hemoptysis eight months before entry. At that time, a diagnosis of tuberculosis was made, followed by hospitalization, and a careful study, which, so far as I can tell, very definitely ruled out tuberculosis. I have no idea what the final diagnoses on discharge from the sanatorium were,

except that fungous infection was considered. The patient returned to work four months later and remained there for two months, after which he was forced to retire. Eight weeks before admission, he developed a dull aching pain in the left chest; night sweats also appeared. The pain was in the axilla and radiated down to the forearm. The patient had fever and lost 10 pounds in weight.

Examination was negative except for local findings in the upper third of the left chest, with dullness and diminished breath sounds. No rales could be heard.

The blood and laboratory findings were entirely negative. X-ray study showed the findings that have been pointed out. The patient had, in addition, a final appearance of Horner's syndrome. It was not a complete Horner's syndrome, at least according to physical examination, since only the smallness of the pupil on the left side was noted. Nothing is said of lidlag or of enophthalmos, both of which are customarily seen with Horner's syndrome.

Our problem is to decide whether this is infection or tumor, and if it is tumor, whether it is a growth within the lung itself. The recurrence of symptoms eight months before entry, with dull pain in the shoulder, is not characteristic of tuberculosis or of any infection. I am inclined to rule out infection, which if present does not seem to be an important part of the picture, and believe that we are dealing with a tumor mass within the chest.

The pain in the upper left chest, the radiation of pain down the arm and the development of a Horner's syndrome immediately make us wonder whether we are dealing with a Pancoast tumor. Pancoast,<sup>†</sup> in his original description in 1924, reported 4 cases, in 2 of which autopsies were performed. Both were first thought to be epitheliomas but were finally diagnosed as squamous-cell carcinomas. Pancoast defines this particular tumor clinically. It must be an extrapulmonary tumor and must show no evidence of origin from the lung or bronchus. It must present erosion of the bone, in addition to pain in the shoulder and axilla that radiates down the arm, with wasting of the muscles of the hands. In all Pancoast tumors, small shadows in the far apex of the lung are visible by x-ray examination.

We must distinguish between the Pancoast tumor and the Pancoast syndrome, which we know today is caused by tumors other than those he originally described. Pancoast's final analysis was that the tumors that arose outside the

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horax, in the superior pulmonary sulcus, originated from embryonic rests of the fifth bronchial left. Other conditions will produce the syndrome. They may be tumors arising in the spinal canal from the meninges, or metastatic lesions in the lymph nodes of the neck. These can be fairly well ruled out in this case. Therefore, I get the impression that we are dealing with an intrathoracic and intrapulmonary tumor, rather than extrapulmonary tumor of the Pancoast type.

If we believe that we are dealing with a tumor within the chest, what is our diagnosis? Is this a benign tumor or a malignant one? The character of the x-ray shadow is certainly suggestive of something with a sharply defined border, which was progressive in size and which was certainly not destructive, so far as the bone was concerned. The tumor mass invaded vital structures outside the lung itself and must have involved the dorsal sympathetic chain and dorsal roots of the eighth cervical nerve or the brachial plexus itself to account for pain that went down the arm. Neurofibroma might be considered. A benign tumor causing little or no bony destruction may produce a Horner's syndrome and could account for the symptoms presented here. It might be endothelioma. Pancoast thought that his original tumors were endotheliomas but changed his mind. They may appear in the pleura, may invade lung tissue and may cause symptoms like those seen in this case.

Fibrosarcoma or any variety of sarcoma might possibly explain the character and symptoms of this tumor. But this tumor appears primarily as apical and less mediastinal, where the fibrosarcomas commonly arise. I do not believe that any of these tumors explain the symptomatology. I think the first two symptoms of importance in this case are pain extending down the shoulder and arm, and hemoptysis. With the presence of hemoptysis, we must presuppose that there is some where a lesion in this patient developing within the bronchus or eroding the bronchus and causing an intraluminal lesion that produced the symptoms. We come down to the final diagnosis which is certainly not Pancoast tumor. It is my impression, from the early history of hemoptysis and pain in the chest and arm, that we are dealing with bronchiogenic carcinoma of the apex of the lung, in the upper lobe bronchus. It grew relatively slowly, and was most likely a squamous cell carcinoma, showing some necrosis in the center to account for the areas of rarefaction. There must have been involvement of the dorsal chain of the left second and third ribs and invasion of the

eighth cervical nerve or of the bronchial plexus itself.

DR DONALD S. KING: As Dr. Badger has said, the important thing was the dark red sputum every day for eight months, which rarely occurs, except with bronchiogenic carcinoma.

DR EDWARD D. CHURCHILL: One of the presenting clinical manifestations in this case was the well being of the patient, who had no cachexia and no sign that is ordinarily seen with long standing illness. The point in differential diagnosis that puzzled me most was the choice between a true intrapulmonary malignant tumor and one arising outside the lung. We might have gained some more information by an artificial pneumothorax, but since the question of operability required an absolute answer, we went ahead with exploratory thoracotomy, with the provisional diagnosis of primary bronchiogenic carcinoma invading the chest wall. The pain in the arm was interpreted a bit differently from the way in which Dr. Badger analyzed it, possibly because we could determine that it was sharply localized to the distribution of the axillary branch of the second intercostal nerve. The statement that the pain was below the elbow was, I believe, incorrect. Cancer, with unmistakable evidence of nerve involvement, is usually out of bounds surgically. This proved to be so when the tumor was disclosed at operation. The growth invaded the chest wall and was clearly of intrapulmonary origin. A frozen section biopsy confirmed the diagnosis of carcinoma.

The problem was one of palliation rather than cure. We know from having seen a great many of these patients with apical carcinoma that the pain in the terminal stages is one of the worst experiences that a person must endure. There has been no way of relieving this pain by section or injection of nerve roots, and the only thing possible is high chordotomy, with its attendant hazards not only to life but loss of sphincter control and other disagreeable sequelae. In spite of the fact that the tumor had invaded the chest wall and despite the fact that there was an involved lymph node 2 cm in diameter in the anterior mediastinum, the lung in this case was removed with the hope that we should then be able to give effective deep x-ray therapy to the chest wall. X-ray therapy with the huge tumor in situ might well have produced necrosis, sequestration and secondary infection of the necrotic tumor mass. The hilum of the lung was free and contained grossly no involved lymph nodes so that the left lung was removed.

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which her temperature was normal and her light constant. She vomited several times, but vomitus was never blood stained.

Abdominal exploration was carried out on the th day.

#### DIFFERENTIAL DIAGNOSIS

DR. MARGARET GLENOY: This baby was brought the hospital because of blood-stained vomitus. cording to the history the vomiting of blood urred only on two days—the third and fourth ys of life. The most frequent cause of vomiting the newborn infant is hemorrhagic disease. There y have been a slight tendency toward hemor- agic disease in this case, but it was certainly t very great. The baby may have been breast t, and some of that blood may have come from icked nipples, but a large dark-red clot would ve been most unusual. The other thing that e would wonder about even in a newborn y is vomiting from esophageal varices. Several ol examinations were made between the fourth d tenth days of life, and none showed any blood. ey may not have been examined at the begin- ag of the hospital stay. Obviously, there was no strointestinal obstruction, and the stool forma- n was fairly normal, because it is not com- ented on after the passing of the meconium.

The outstanding abnormal finding in this rec- d is the mass in the left flank. Apparently, it d not extend beyond the mid-line. There was a lge in the flank, but no comment of any bulg- g posteriorly in the loin. Taking the meaning the words literally, I am inclined to think first all of an enlarged spleen. With an enlarged leen, the first thing that comes to mind is eryth- blastosis fetalis. This baby's blood smear owed only one nucleated red blood cell per 100 . Also, there is no comment that the vernix was lden yellow, and no mention of a large heart; scarred placenta is not mentioned. Nothing is own about the nationality of the parents, so far

the late type of erythroblastic anemia is con- rned. The spleen might have been enlarged :cause of sepsis, but there was no fever and no ukokytosis, and the differential count of the fifth x sixth day is not abnormal. The spleen might ve been enlarged because of congenital syphilis. owever, x-ray examination of the long bones was egative. No mention is made of the mother's lood Hinton reaction. Nothing is said about arasites in the blood smear. The baby might ve had congenital malaria. I do not believe that e did, however. She had no temperature rise in n days, but the absence of temperature rise does

not preclude the possibility of infection or even sepsis in a newborn infant.

I am not certain about the urinary-tract exam- ination. The pyelogram showed no excretion from the left kidney. On the basis of one pyelo- gram, I am not convinced that the tumor was renal in origin. There may have been only one kidney, but it may be that in the x-ray film the density of the mass in the left flank made the slight amount of concentration of the dye in the pelvis invisible. If this were a kidney tumor of a non- functioning kidney, one would expect to find a rather round mass, and one would also expect to find some mass in the loin. Polycystic kidneys are usually bilateral. Solitary cysts of the kidney are, statistically speaking, more frequent on the right than on the left. The Wilms tumor is the most usual kidney tumor in childhood. Sarcoma of the kidney might have invaded the vena cava in utero, producing obstruction and hence collateral circulation and bleeding from varices. Another thing against kidney tumor is the statement that the tumor was freely movable.

Abdominal exploration was carried out. One would not operate on a baby with a large spleen just because it extended from the brim of the pelvis to the thoracic cage. One would operate because there was something there that might inter- fere with the existence of that child. I have not seen the x-ray films, but my conclusion is that this baby had neoplasm of the spleen. I do not know what the type of growth was.

DR. TRACY B. MALLORY: Should you care to see the x-ray films?

DR. GLENOY: I should like to very much.

DR. JAMES R. LINGLEY: The x-ray films are quite helpful in this case, I think. They show quite definitely that this was a tumor of the kidney and not of the spleen, because on the plain film one can see a perfectly normal spleen above the mass that occupies the whole flank. This mass is very large, extending from under the costal border to the crest of the ilium and well over to the mid-line. The pyelogram shows a normal kidney on the right, with good excre- tion of the dye and absolutely no excretion on the left side. So that I consider the x-ray evidence definitely in favor of a tumor of the kidney. The lungs show nothing definite.

DR. MALLORY: Do you want to accept the x-ray evidence, Dr. Glendy?

DR. GLENOY: Certainly; I am very grateful for it.

DR. MALLORY: It is not always wise.

DR. GLENOY: May I ask why they operated?

Was the baby not doing well from any other point of view?

DR. SIDNEY FARBER:\* No; they operated for one good reason: the nature of the large firm mass in the left flank could not be determined without surgical intervention.

DR. FLETCHER H. COLBY: In babies with enlarged spleens, do you ever find that the enlargement is sufficient to cause nonfunctioning of the kidneys? Does it always cause displacement, but not nonfunctioning?

DR. FARBER: Disturbance of kidney function caused by an enlarged spleen must be extremely rare.

#### CLINICAL DIAGNOSIS

Hemorrhage into left adrenal gland.

#### DR. GLENDY'S DIAGNOSIS

Congenital tumor in left flank, probably arising from spleen.

#### ANATOMICAL DIAGNOSIS

Neuroblastoma sympatheticum of left adrenal gland.

#### PATHOLOGICAL DISCUSSION

DR. FARBER: Many years ago, I learned by sad experience that it was unwise to take too seriously clinical palpation of the notch of the spleen as evidence that a mass in the abdomen represented the spleen. The report in the history of the palpation of a notch was definitely misleading. The patient under discussion today was seen in 1933. For that reason, no information such as might be obtained today concerning the nature of the hemorrhagic episode observed soon after birth is available. I believe that Dr. Glendy's choice of hemorrhagic disease with spontaneous improvement is probably the correct explanation for the vomiting of blood. The surgeon, Dr. George Cutler, resorted to operation because the nature of the large mass that was palpated could not be determined by any clinical or roentgenologic method of study with any degree of accuracy. The clinical diagnosis was massive adrenal hemorrhage. The presence of a malignant tumor was suspected. At operation, Dr. Cutler removed a mass that lay immediately above the left kidney replacing the adrenal gland. It was completely encapsulated and could be stripped without difficulty from the surrounding structures. It

weighed over 100 gm. and was round and smooth, and the capsule was intact. The cut surface disclosed a mass divided into a number of lobules containing hemorrhagic necrotic tissue. The final pathological diagnosis was neuroblastoma sympatheticum, which had undergone extensive hemorrhagic necrosis.

The subsequent story may be of some interest. The infant recovered soon after the operation; eight years after that procedure, the child is still alive and in good health. Certainly, the patient has passed far beyond the point where metastasis or recurrence might be expected. I might add that no radiation or any other treatment directed at the tumor was employed at any time.

I should like to make some remarks concerning one of the questions that arose in the matter of differential diagnosis. The pyelogram is of no real aid in the accurate diagnosis of tumors of the kidney region in early life, and may indeed mislead the surgeon if too much reliance is placed on interpretation of the x-ray films. In the first place, it is impossible to tell by means of the pyelogram whether the tumor is within the kidney or within the adrenal gland, or whether the tumor is unattached in the region of the kidney. A neuroblastoma arising from the adrenal medulla may cause just as much obstruction to the ureter as an embryoma arising within the kidney. Furthermore in 3 cases, I have seen a neuroblastoma arise from an adrenal gland in which the growth rested within the substance of the kidney and was responsible for an x-ray picture and a gross pathologic specimen that could not be differentiated from an embryoma of the kidney. In the second place, it is of little importance to know before operation whether the mass is within the kidney or in the immediate vicinity of the kidney. The exact location of the tumor must be determined by the surgeon at the time of operation. The only real use for a pyelogram in infants or children suspected of having a tumor in the kidney region is to provide an easy method of demonstrating that two kidneys are present, in the event that the surgeon must remove one kidney with the tumor.

A second point worthy of special emphasis concerns the reason for operation and exploration of the abdomen of this young infant in whom the main finding was a mass in the abdomen. For many years, we have been guided by Dr. S. Burt Wolbach's generalization concerning tumors of early life, which has been well borne out by repeated tests. This is: *every solid mass in early life is to be regarded as a malignant tumor until*

\*Assistant professor of pathology, Harvard Medical School; pathologist, Children's Hospital.

*proved otherwise by pathological examination* Although blanket rules are at times quite dangerous, this generalization has settled many a discussion concerning the proper method of treatment in problems of this kind and has not led us into erroneous or harmful decisions

By neuroblastoma sympatheticum I mean the malignant variety of the series of tumors arising in the sympathetic nervous system The true nature of this tumor, incidentally, was demonstrated at the Massachusetts General Hospital by Dr Jomer Wright in 1911 In a series of 40 neuroblastomas, which occurred in a ten year period at the Boston Children's Hospital, more than half arose in situations outside the adrenal medulla About one fourth of these 40 patients are alive and apparently well after operative removal of the tumor and histologic verification of its nature The tumor is extraordinarily radiosensitive In 2 cases, cures have been obtained by means of radiation therapy after metastases to the liver had been proved

by histologic study My experience in recent years has led me to conclude that the opinion in the literature concerning the almost universally bad results with the neuroblastoma is not a correct one At the present time, the method of choice in the treatment of the neuroblastoma is removal of the primary tumor, with subsequent radiation of the area involved by the tumor Radiation therapy should also be applied to areas involved by metastatic tumor

A PHYSICIAN. How often are tumors of the adrenal gland as readily movable as the one described in this case?

DR. FARBER. Not often. If the tumor is readily movable, it is more apt to be one arising in the periadrenal tissues rather than in the adrenal gland or in the kidney tissue.

A PHYSICIAN. Was the kidney involved?

DR. FARBER. No; it was just pushed aside by the tumor mass

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## COMBINED SEROTHERAPY AND CHEMOTHERAPY IN PNEUMONIA

SINCE the introduction of effective sulfonamide drugs, the question of whether specific antipneumococcus serums have any further place in the treatment of pneumonia has been the subject of great controversy. Most physicians may no longer consider this problem of any importance, since they are only occasionally called on to treat patients who are severely ill with pneumonia, and since they have already had an opportunity to convince themselves of the effectiveness of sulfapyridine and sulfathiazole in their cases.

Physicians who treat large numbers of cases, however, are still confronted with some patients

whose response to drug treatment is not entirely satisfactory. There are two schools of thought with respect to the additional use of serum in these cases. In one group are those who, like Janeway and Beeson,<sup>1</sup> believe that the additional use of serum in such cases increases the chances for recovery and shortens the duration of acute illness. They recommend the combined use of chemotherapy and serotherapy as the most satisfactory form of treatment in severe pneumonia. In the other group are a large number with a growing conviction that serums have little or nothing to offer in cases in which sulfonamides alone fail. Each of these views has had strong support from controlled clinical studies, which have been recently published. Two reports in particular may be mentioned.

Dowling, Abernethy and Hartman<sup>2</sup> studied a series of patients with Type 1 through Type 8 pneumonias who were alternated for treatment with sulfapyridine alone and with sulfapyridine in addition to specific antipneumococcus serum. Treatment was begun in each therapeutic group as soon as the type was determined. The mortality rate was 12.5 per cent in the group receiving sulfapyridine alone, and 9.8 per cent in the group receiving serum and sulfapyridine. When the Type 3 cases were omitted, the mortality was 9.2 per cent in patients treated with the drug alone and 4.5 per cent in those who received serum in addition. Serum was found to be particularly valuable as an adjunct to sulfapyridine in patients over forty years of age. Crisis occurred more frequently and was prompter in the patients receiving serum in addition to sulfapyridine. These authors suggested that the combined use of serum and chemotherapy be given to patients with pneumonia who are over forty years of age and also to those who are in need of a prompt defervescence.

Those who are not enthusiastic about the use of serum and who consider that its cost and the additional expenditure of the time and effort required in its use are not justified by the additional benefits to the patient may take solace in a re-

port by Plummer and his associates<sup>3</sup> at Bellevue Hospital. These authors used a number of sulfonamides and alternated all patients for treatment by type between chemotherapy with one of these drugs alone and combined chemotherapy and serotherapy. In this study, the results were the same in both groups, regardless of whether the patient was treated early in the disease, whether bacteremia was present, whether the patient was old, and whether systemic disease was present. The authors are, however, willing to concede, "There will probably be no disagreement with the statement that serum should be used for patients who cannot tolerate the sulfonamide drugs or for those who fail to respond satisfactorily within twenty-four to forty-eight hours to drug therapy." They also mention that in their private practice they have used serum several times with gratifying results for patients who failed to respond to chemotherapy, although obviously they cannot say whether these patients would not eventually have recovered without the use of serum.

Finland, in this issue of the *Journal*, points out some of the difficulties involved in carrying out carefully controlled clinical studies on the use of serums. A number of the pitfalls in the Bellevue study are mentioned, and many more can be found on careful perusal of the data presented. Certain important information is also lacking. In particular, the alternation of cases by type could not have been so strict as the authors claim and yet have the series end with 6 more Type 2 patients and 4 more Type 13 cases in one or the other of the two groups. Furthermore, drug treatment was started in all cases immediately, and alternate patients were placed in the serum-plus-drug groups after the type was determined, regardless of whether it was unnecessary to administer serum, because the patient was dead or well. It is stated that the interval between the start of the drug treatment and the time serum treatment was begun was "usually within the first twenty-four hours." Since it is known, however, that the vast majority of patients with pneumonia who eventually respond to chemotherapy already

give clear evidence of a favorable response within this period, it is obvious that those who actually received serum were, in most cases, the patients who had responded poorly to chemotherapy.

Although the conclusions drawn by the Bellevue workers from these cases may or may not prove to be correct, Finland points out that the results of studies of this sort are "not only inconclusive but even grossly misleading," since they make unwarranted claims of scientific control. The results here, as in many other studies, are influenced by important factors in the choice of cases that are either unrecognized or merely ignored. Obviously, the "choice" is usually exercised unconsciously.

Combined serotherapy and chemotherapy will certainly not be used routinely by the vast majority of physicians. It is only in the severe cases and in those patients who are unable to tolerate the sulfonamides that the early use of serum in addition to the drug is justified. The usefulness of serum when the drugs fail is generally conceded.

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- 2 Dowling, H. F., Abernethy, T. J., and Hartman, C. R. Should serum be used in addition to sulphydryl in the treatment of pneumococcus pneumonia? *J. A. M. A.* 115:2125-2128, 1940.
- 3 Plummer, N., Liebmans, J., Solomon, S., Kammerer, W. H., Kalkstein, M., and Ensworth, H. K. Chemotherapy versus combined chemotherapy and serum in the treatment of pneumonia: a study of 607 alternated cases. *Ibid.* 116:2366-2371, 1941.

#### DIRECTORY OF MEDICAL SPECIALISTS

THE second edition of the *Directory of Medical Specialists*, which will be ready for distribution in February, 1942, will list the names of approximately 18,000 diplomates of the fifteen American boards that examine candidates for certification in the specialties; this is 4000 more than were included in the first edition, which was published early in 1940.

The geographic grouping will give completely revised biographic data about each diplomate, including much information not found in the first edition, such as military appointments and the details of formal training. In addition, the plan of organization, the officers and the examination

requirements of each American board will be fully outlined.

The *Directory* again presents a list of physicians and surgeons who have had excellent training and adequate experience in their chosen fields and who have limited their practice to those fields. This official record of specialists is invaluable as a reference: it provides essential data concerning qualified specialists throughout the United States and Canada, information that is extremely useful to the officers of medical societies and to physicians who refer patients to associates in distant communities.

The new edition will probably be as much in demand as its predecessor, which had a wide distribution, not only among the members of the medical profession and medical libraries, but also among insurance companies and firms that manufacture and distribute medical supplies.

## MEDICAL EPONYM

### KERNIG'S SIGN\*

Vladimir Michailovich Kernig (1840-), ordinator at the Obuchow Hospital in St. Petersburg, reported "Ueber ein wenig bemerktes Meningitis-Symptom [A Little-Noticed Symptom of Meningitis]" in the *Berliner klinische Wochenschrift* (21: 829-832, 1884). A portion of the translation follows:

For a number of years, I have noticed in the cases of meningitis that have come under my attention a symptom that seems to be little known, although in my opinion it has a definite, practical value. I refer to the occurrence of a flexion contracture in the legs, occasionally occurring also in the arms, which is first seen when the patient sits up. . . . If the patient sits on the edge of the bed so that the legs hang over (in cases with very marked stiffness of the neck and back this is not easily accomplished), the contracture of the neck and back usually becomes much more marked. Furthermore, there is now observed a flexion contracture in the knee joint and occasionally, also, in the elbow joint. Extension of the patient's leg at the knee is now only possible to an angle of about 135°, or if the phenomenon is marked, only to a right angle. . . . I am also convinced that, with the patient in the dorsal position, this contracture appears when the extended leg is brought to a right angle with the trunk. In normal patients, no similar contracture is seen with the same degree of flexion of the hip.

R. W. B.

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

#### FATAL DIABETIC COMA IN PREGNANCY

A thirty-year-old para II was first seen when she was approximately thirty-two weeks pregnant. She had had diabetes for ten years and had been followed by a hospital clinic. She had always been most unco-operative and had been in the hospital in diabetic coma twelve times prior to the present admission. The previous pregnancy terminated in a premature breech delivery at six months. The baby was stillborn, and the patient herself was in diabetic coma.

The patient was kept in the hospital about three weeks. At the end of this time, since she was somewhat over thirty-six weeks pregnant, it was decided to deliver her by cesarean section and sterilize her. She was presumably in good condition from the standpoint of the diabetes on the morning of operation. After the administration of 3 gr. of Nembutal and 15 cc. of paraldehyde in oil, she was taken to the operating room. Her condition suddenly became extremely serious, and the blood pressure dropped to 82 systolic, 50 diastolic, and the pulse rose to 172. The operation was postponed, and on the same afternoon the blood pressure rose very suddenly to 202 systolic, 90 diastolic. The patient developed a right-sided facial paralysis and died undelivered.

*Comment.* Pregnancy in diabetes is much more frequently seen than it was in the preinsulin days, and a death such as this should be extremely unusual. Well-organized diabetic clinics have no fear for the mother's life. Not yet can a living baby be guaranteed in every diabetic pregnancy. It is true that this patient was most unco-operative, but in the light of the experience of other diabetic clinics it does seem that this maternal death could be attributed solely to unskilled handling of the diabetic problem. The average practitioner has learned that insulin almost always controls diabetes very easily. The average diabetic specialist who has not seen much of the complication of pregnancy does not appreciate the instability that pregnancy places on these patients. This can fairly be called a preventable death. If deaths occurring in diabetic patients during pregnancy are to be prevented, the pregnancies of these patients must be handled by trained diabetic specialists and those who have had particular experience in handling the problem.

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, Secretary, 330 Dartmouth Street, Boston.



## DEATH

September 11, 1941

FULLER—ERNEST P FULLER, M.D., of Lawrence, died September 14. He was in his sixty ninth year.

Born in North Andover, he graduated from New York University College of Medicine in 1899. Dr Fuller was on the staff of the Lawrence General Hospital, and was a fellow of the Massachusetts Medical Society and the American Medical Association. He held memberships in the Lawrence and North Essex medical clubs.

His widow, a daughter, three grandsons, three sisters and a brother survive him.

## NEW HAMPSHIRE MEDICAL SOCIETY

## DEATHS

ABBOTT—CHARLES B ABBOTT, M.D., of Hillsboro, died March 24. He was in his seventeenth year.

Dr Abbott, the son of Benjamin and Mary (Choate) Abbott was born in Bradford and graduated from Dartmouth Medical School in 1902. He was a member of the New Hampshire Medical Society.

He is survived by his widow and a sister.

WEINBERG—PHILIP B WEINBERG, M.D., of Whitefield, died August 27. He was in his fifty fourth year.

Born in Berlin, Germany, Dr Weinberg received his degree from Tufts College Medical School in 1920. He was a member of the New Hampshire Medical Society and the American Medical Association.

He is survived by his widow, three brothers and three sisters.

## CORRESPONDENCE

## COMBINED SEROTHERAPY AND CHEMOTHERAPY IN PNEUMONIA

To the Editor: In the paper entitled, 'Controlling Clinical Therapeutic Experiments with Specific Serums,' which appears in this issue of the *Journal*, is included a criticism of a study that was published from Bellevue Hospital. In view of this, I took the liberty of sending a copy of the manuscript to Dr Norman Plummer, prior to publication, and have received the following reply: 'I believe it is only fair that you publish this letter, and you have Dr Plummer's permission to do so.'

I believe that the arguments brought forth by Dr Plummer serve only to emphasize the whole theme of my discussion, namely, that it is impossible to carry out large scale clinical experiments with strictly scientific controls that are not open to criticism. As a single example, if one works out the probability that the difference in the twenty four hour deaths in the two groups is a matter of chance, one finds that it is approximately one out of thirty five times.

It is only because we have ourselves been so thoroughly disillusioned when reviewing the results of our clinical results, which we thought were carefully controlled, that we became convinced of how difficult it is to carry out such experiments.

MAXWELL FINLAND

Boston City Hospital  
Boston

Dear Dr Finland: Your paper arrived a few days ago, and I appreciate your consideration in sending it to me. Perhaps I can clarify some of the points to which you refer in your criticism.

You state, 'Some of the patients were already dead and others were afebrile at the time the type was determined, they received no serum, but were nevertheless retained in the group receiving combined treatment.' The statement implies that this was not the way in which to handle the alternation of cases. The plan we had in mind from the start was to handle the series as though the patients were being treated in two different hospitals. On the shelves of the one hospital there was a supply of sulfonamide drugs, and on the shelves of the other there were both sulfonamide and serum. Everything else was the same for the two groups of cases. In each series the effort was made to obtain the best results possible under the circumstances of the experiment. We realized that one disadvantage of specific serum was the delay in administration caused by the time required for typing. It is true that a few (6) patients dying within twenty four hours were dead before the typing was obtained. Should these cases have been removed from the series? To do so would not be legitimate unless the cases in the chemotherapy alone series were treated in the same way, and any attempt at such manipulation would certainly be open to criticism. Some patients (actually 95 of the 301 cases) were so fully recovered that, when the typing was obtained serum was no longer indicated. The serum was available had there been any use for it. What should be done with these cases? To remove them, and to offset this by removing similar cases from the other group, again would be difficult and would be a manipulation of the experiment.

You state, 'It is rather odd, in view of the strict alternation in type stressed by these authors, that for many of the types there is a preponderance of cases either in the series treated with the drug alone, or in the combined therapy series.' By this, you refer to there being in Type 2, 49 cases on the one side and 55 on the other, in Type 5, 24 and 27, in Type 13, 5 and 1, in Type 18, 3 and 6, in Type 19, 8 and 5, and in Type 20, 7 and 4. This discrepancy can be quickly explained while we used strict criteria for making the clinical diagnosis, there were cases included and alternated that, on later analysis, were proved not to have pneumonia. This was particularly striking in Type 2, because during one season there was a high incidence of Type 2 pneumococci in severe upper respiratory infections. Furthermore, our experiment was opened and closed three different years, which again created some of this discrepancy.

Again you state, 'The length of the delay before serum treatment was given in most cases is not mentioned.' The typing was done in a pneumonia laboratory by experienced technicians giving a twenty four hour service. Emphasis was placed on rapidity and accuracy. The delay in obtaining types was probably equal to that which you encounter on your service and much less than that in the average large hospital. Because of the quality of typing service which we maintained, the results obtained in our combined group should have been better than would have been expected were the typing less efficient.

You continue with this statement, 'Furthermore, although mention is made of the number of patients who received serum and died within twenty four hours, the total number of patients who actually received serum

is not given." You failed to get the important point of our study: namely, that we were not comparing the results with serum and no serum, but the results in a series of having the benefits of both drug and serum with those in a series having only the drug. Actually 62.4 per cent of the patients in the serum series received serum, and only 6 of the cases due for serum died before it could be given.

Your next statement is, "Moreover, a considerable portion of the mortality among the patients who received combined treatments occurred within twenty-four hours of admission to the hospital, whereas only a small number of those receiving drug alone died within twenty-four hours of entry." This was exactly the way the series turned out, and it shows how the laws of chance operate in such a study. The fallacy of including the twenty-four-hour deaths is well recognized, and that is the reason why we show these cases apart from the rest of the series.

You further state: "... it seems much more probable that some unconscious selection on the part of the authors played an important role in the inclusion of the poorest subjects among the serum recipients. This is only a natural occurrence, since there is always a tendency to give to the patients who seem the most severely ill the benefits of any remedy that is known to be effective." We avoided such a possibility by taking a number of precautions. There were a number of physicians treating the patients, and they had nothing to do with the alternation of the cases. This was done in the laboratory by the technicians, who again had no knowledge whatever of the clinical condition of the patients. Furthermore, the serum was kept in the laboratory and delivered to the ward when a serum case was discovered. On this basis, how there could have been a conscious or unconscious selection, I am at a loss to explain. With such criticism as you did offer you must consider the possibility of manipulation at the time the list was compiled. Actually, the list was compiled by seven different persons, and at the time the columns were added no one had the slightest conception of how the series turned out.

Finally, you conclude, "The conclusions drawn by these authors may or may not prove to be correct, but one cannot help believing that the results as presented are not only inconclusive but are even grossly misleading." If you will reread the paper, you will note that we avoid sweeping conclusions.

I was amused at your final paragraph, in which you say, "It is my opinion that this particular question as it concerns pneumonia is now a highly academic one, since it is unlikely that any physician would contemplate using the combined therapy as a routine in all cases." Originally, we concluded our paper with: "Our results indicate that serum no longer plays a role in the routine treatment of pneumonia," but we thought that this statement was too strong. In presenting our study, we had no desire to draw conclusions, but we did make every effort to tabulate our results as accurately as possible. The omission of the figures mentioned by you was not done to mislead anyone, but to make the article as concise and brief as possible. There was not a single individual in our group who had a preconceived opinion regarding the outcome of the investigation. All of us had used serum enthusiastically and had no reason to oppose its use. Furthermore, our active group received constant counsel from the directors of our divisions, Dr. Cecil and Dr. Sutliff, and it hardly seems possible that they would allow us to be so "grossly misleading."

I have tried to answer your criticism as completely as possible, but if there is any point which is not entirely covered, I shall be pleased to discuss it further with you.

Yours sincerely,

NORMAN PLUMMER

The New York Hospital  
New York City

## NOTICES

### ANNOUNCEMENTS

DR. HILBERT F. DAY announces the removal of his office from 412 Beacon Street, Boston, to 34 Kirkland Street, Cambridge.

DR. LEO J. McDERMOTT announces the removal of his office from 372 Longwood Avenue, Boston, to 151 Vaughan Street, Portland, Maine.

DR. AUGUSTUS RILEY announces the removal of his office from 868 Beacon Street to 59 Bay State Road, Boston.

### JOHN T. BOTTOMLEY SOCIETY

The regular monthly meeting of the John T. Bottomley Society will be held in the Out-Patient Building of the Carney Hospital on Wednesday, October 1, at 11:30 a.m.

Physicians and students are cordially invited to attend.

### BOSTON DOCTORS' SYMPHONY ORCHESTRA

The Boston Doctors' Symphony Orchestra will resume rehearsals, under Alexander Thiede, on Thursday, October 9, at 8:30 p.m. at Station WMEX, 70 Brookline Avenue, Boston. Those interested in becoming members should communicate with Dr. Julius Loman, 520 Beacon Street, Boston (KEN 3200 or LON 2155).

### CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Haverhill	October 1	William T. Green
Lowell	October 3	Albert H. Brewster
Salem	October 6	Paul W. Hugenberg
Brockton	October 9	George W. Van Gorder
Gardner	October 14	Mark H. Rogers
Northampton	October 15	Garry deN. Hough, Jr.
Worcester	October 17	John W. O'Meara
Pittsfield	October 20	Frank A. Slowick
Fall River	October 27	Eugene A. McCarthy
Hyannis	October 28	Paul L. Norton

### WACHUSETT MEDICAL IMPROVEMENT SOCIETY

The next meeting of the Wachusett Medical Improvement Society will be held at the Holden District Hospital on Wednesday, October 1, at 6:30 p.m. Dr. Richard Schatzki, of the Massachusetts General Hospital, will speak on "X-Ray Examination in Cases of Hemorrhage from the Upper Gastrointestinal Tract."

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## CARCINOMA OF THE LUNG: BRONCHOSCOPIC ASPECTS\*

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**B**RONCHOSCOPY is the most important method of diagnosis in primary carcinoma of the lung. Such new growths appear to be on the increase and now cause from 8 to 18 per cent of all deaths due to cancer, as reported by Jaffe,<sup>1</sup> Kolesky,<sup>2</sup> Simons,<sup>3</sup> Graham,<sup>4</sup> and Ochsner and DeBakey.<sup>5</sup> Approximately 75 per cent of such tumors arise in the major bronchi, as shown by Tuttle and Womack,<sup>6</sup> Gebauer,<sup>7</sup> Broyles and Fisher,<sup>8</sup> and Overholt and Rumel.<sup>9</sup> Lesions so situated can be visualized and biopsied bronchoscopically.

In 1933, before the advent of pneumonectomy for cancer of the lung, bronchoscopic investigation of such cases was infrequent. The high percentage of positive diagnoses that would be obtained by his method of investigation if all persons suspected of having pulmonary neoplasms were studied endoscopically is still not generally appreciated. In 1939, Taylor<sup>10</sup> stated that "confirmation of lung tumors is not usually available preoperatively. . . ." This statement may have been true, but need not be true today if all patients with unexplained pulmonary symptoms are studied bronchoscopically.

The patient with a change in bowel function rightfully deserves a proctoscopic examination. Abnormal urinary symptoms often indicate the desirability of cystoscopic studies. Likewise, the patient with unexplained pulmonary symptoms cannot be considered fully investigated without a bronchoscopic inspection of the trachea and bronchial tree.

Establishing a verified diagnosis of cancer at an early stage of the pathologic process should not be so difficult in neoplastic lesions of the lung as in other internal organs. In a personal series of 62 cases with histologically verified primary neoplasms of the lung, the lesion was seen and a positive preoperative diagnosis of cancer made from the biopsy specimen in 46 cases (74 per cent). In con-

trast with this, cancers of the kidney, gall bladder, pancreas, stomach, brain or colon, with the exception of the rectum and sigmoid, are practically never histologically verified before exploration. The high percentage of preoperative positive biopsies in cases with a pulmonary neoplasm should make this lesion one of the most favorable types. This report is presented to demonstrate the value of bronchoscopy in the diagnosis of pulmonary tumors and its application to the determination of operability and expedition of therapy.

### PRESENT-DAY BRONCHOSCOPIC EXAMINATION

Endoscopic investigation of the tracheobronchial tree should not be delayed because of hesitancy on the part of the physician or fear on the part of the patient. It is not an ordeal to be endured, but rather it is an examination that can be performed easily under local anesthesia, with minimal discomfort and with little inconvenience to the patient. Therapeutic bronchoscopies may be satisfactorily managed in an outpatient department, but diagnostic investigations are preferably done as a hospital procedure. The patient is admitted the day before and is ready for discharge the day following the examination. Such a routine permits adequate investigation and preoperative medication, the latter being a valuable adjunct to local anesthesia. Patients are taken to the operating room conscious, but relieved of the sense of anxiety and fear by a barbiturate two hours previously, and by morphine and scopolamine subcutaneously one hour preoperatively. Topical application of cocaine or Larocaine to the hypopharynx and each pyriform sinus is supplemented by the intratracheal instillation of a few cubic centimeters of a diluted solution of the same agent. Painful impulses from the upper respiratory tract are thus abolished, the irritative sensation of a foreign body in the tracheobronchial tree is alleviated, and the cough reflex is suppressed.

Proper teamwork is essential for this type of

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endoscopic work. Inadequate preparation, inexperience and lack of teamwork on the part of the operator and assistants are responsible for the common misconception that bronchoscopic examination is a severe ordeal for the patient. With the patient in the dorsorecumbent position, with the head and shoulders projecting over the end of the table, the head is held forward and extended on the cervical vertebrae. In this position, a straight line is formed from the open mouth to the trachea. A straight, nonflexible tube, such as the bronchoscope, can then be inserted into the trachea without trauma.

A careful and complete examination of the trachea and the visible portion of the bronchi can be carried out in a few minutes. A definite routine of inspection, including examination of all major bronchi, should be followed to obtain all the information possible. Patients frequently express surprise at the lack of discomfort, and in many cases they do not even remember the procedure the following day, especially if scopolamine has been administered preoperatively. When the investigation is performed carefully, it is practically without risk.

INDICATIONS FOR BRONCHOSCOPY

Bronchoscopic examination is indicated in every patient who is suspected of having a primary pulmonary cancer, except for the patient with obvious widespread metastases. Practically all patients with neoplastic lesions have some respiratory symptom. Ninety-eight per cent of the series reported by Overholt and Rumel<sup>9</sup> had definite symptoms that indicated an abnormality of the respiratory system. They found cough to be the most frequent symptom (87 per cent); fever was next (53 per cent); and chest pain or discomfort was third (44 per cent). Hemoptysis, marked weight loss and symptoms due to metastatic lesions are usually late signs and should not be awaited before institution of adequate investigation. The disease is most frequently encountered in the fourth and fifth decades, but the extremes are not uncommon. The age of the patients in the present series varied from eighteen to sixty-seven years.

It is not the intention of this report to promote the idea that all patients with pulmonary symptoms should have a bronchoscopic examination. However, all patients with unexplained pulmonary symptoms do warrant this investigation. Cases of pneumonia that are atypical and do not respond to the usual therapy in a few weeks may be due to bronchial obstruction by a tumor. Recurrent pneumonia of the same lobe may be due

to intermittent atelectasis of that lobe. Development of a respiratory wheeze, especially in a patient without past allergic history or in one who does not respond promptly to allergic therapy, necessarily places that patient in the class in which cancer is suspected.

The etiologic factor in most pulmonary lesions becomes apparent after a careful history has been taken, after a complete physical examination has been made, and after adequate roentgenologic studies have been secured. Sputum, if obtainable, should always be examined for both acid-fast bacilli and other organisms.

It is the patient who is still not diagnosed after performance of the above studies who warrants bronchoscopic examination. Even a roentgenologic diagnosis of pulmonary cancer is not sufficient, since a verified diagnosis cannot be made by this method. Too often, the physician becomes discouraged and goes no farther after receiving a report of primary lung cancer from the roentgenologist. Furthermore, the extent or operability of a given lesion may be misleading by roentgenography. Bronchoscopy is the most accurate way of determining both these factors.

CLASSIFICATION

From the bronchoscopic viewpoint, pulmonary carcinomas may be conveniently divided into two groups, central and peripheral, depending on the site of origin of the lesion. The central or stem-bronchus group (Figs. 1 and 2) includes those arising in the larger air passages, that is, proximal to the bifurcation of the bronchi of the third order. In other words, these lesions arise in the main bronchus, in the lobar bronchi or in the proximal portion of one of the lobar bronchial subdivisions. Lesions in this central group comprise approximately 75 per cent of all primary neoplasms. If the tumor itself can be seen endoscopically, it necessarily falls in the central classification. Peripheral tumors include all those arising beyond the proximal segment of a bronchus of the third order. They cannot be directly visualized by bronchoscopy, although frequently a deformity of the bronchus may be noted owing to an inward displacement by pressure of the tumor mass. Such an observation is strong presumptive evidence of neoplasm, although tissue may not be obtained for histologic examination. Bronchoscopy is the most accurate way of determining whether the lesion is central or peripheral.

For three reasons, tumors falling in the central group of neoplasms seem more favorable from a therapeutic standpoint. First, a new growth in a major air passage produces symptoms earlier than

one distally situated, since it soon encroaches on the lumen of the bronchus and thus gives rise to symptoms; peripheral tumors usually have to be of considerable size before structures are involved that will cause the patient to realize there is something abnormal. Secondly, lesions arising in main or lobar bronchi can be visualized and

though there was no roentgenographic evidence of disease.

### *In Late Primary Lesions*

As soon as the growth reduces the lumen of the bronchus appreciably, abnormal physical signs and roentgenographic abnormalities appear. From

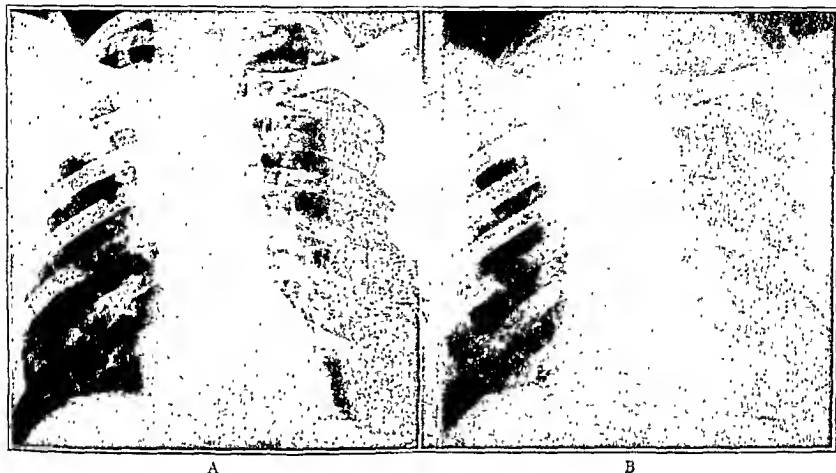


FIGURE 1. Roentgenograms of Chest.

A shows partial atelectasis of the right upper lobe. Owing to the presence of diffuse bilateral calcified foci, the patient was treated for pulmonary tuberculosis in a sanatorium for seven months, in spite of a negative sputum. B, taken six months later, shows progression of the lesion to complete atelectasis. A diagnosis of epidermoid carcinoma was established by bronchoscopic biopsy.

biopsied bronchoscopically, thus permitting an earlier verified diagnosis, with resultant improvement in treatment. Thirdly, there is evidence (Tuttle and Womack<sup>4</sup>) to show that tumors in the central location grow more slowly and metastasize later than lesions situated peripherally.

### USES OF BRONCHOSCOPY

#### *In Early Primary Lesions*

A small submucous bronchial lesion may not produce pulmonary signs or symptoms. When such a tumor extends intrabronchially or breaks through the mucosa, it produces cough or, if ulceration is present, hemoptysis. Depending on the size and configuration of the neoplasm, roentgenographic findings may or may not be present. Few cases are observed at such an early period, yet the lesion may be visible bronchoscopically. In one case in this series, investigated because of hemoptysis, a diagnosis of pulmonary carcinoma was established by bronchoscopic biopsy even

meager physical and roentgenographic findings to most striking signs may represent a very short period in the tumor cycle. When a major bronchus becomes occluded, that portion of pulmonary parenchyma supplied by it becomes atelectatic; hence, marked signs become apparent. The extent of the findings on physical and roentgenographic examinations is not a criterion of the extent of the disease, since a mass 2 or 3 cm. in diameter located in a main bronchus may produce atelectasis of the entire lung. If such a tumor were primarily intrabronchial, it might well not have extended beyond the realm of resectability. Bronchoscopic visualization of the tumor gives a much more accurate knowledge of its extent than either physical examination or roentgenography.

#### *In Metastatic Lesions*

The lungs are frequently the site of metastatic implants from distant organs. As a rule, pulmonary metastases reveal themselves as multiple, well-defined, discrete shadows in the pulmonary

parenchyma and cannot be visualized bronchoscopically. On occasion, an implant may involve the wall of a major bronchus and produce roentgenographic findings of atelectasis, which cannot be differentiated from those produced by a primary bronchiogenic neoplasm.

In two cases, I have obtained positive biopsies bronchoscopically in tumors that were not bronchiogenic in origin. One was a lymphoma with involvement of the left lower-lobe bronchus, and the second was a metastatic implant from a mel-

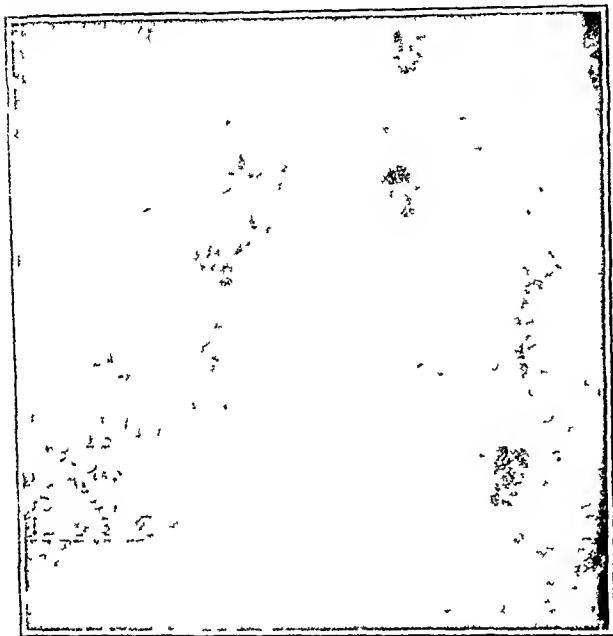


FIGURE 2. Roentgenogram of Chest

*In this patient, who was sixty-seven years of age, with a history of a moderately productive cough of two months' duration, a presumptive diagnosis of bronchiectasis had been made. Bronchoscopic examination revealed a primary bronchiogenic carcinoma. Note the haziness of the right lower lung field. Pneumonectomy was successfully performed.*

anotic sarcoma of the eyelid, the original tumor having been removed four years previously.

#### Other Uses

Bronchoscopy should not be limited to the one function of establishing a histologically verified diagnosis. Information of great value in determining the plan of treatment can be obtained by a complete bronchoscopic visualization of the trachea and major bronchi.

**Determination of operability.** Radium, roentgen rays and surgery are the three methods available for treating primary carcinoma of the lung. Reports have appeared in the literature by Leucutia,<sup>11</sup> Brock<sup>12</sup> and Leddy and Moersch<sup>13</sup> of five-year cures by radium or roentgen-ray therapy, or

both. Surgery, by far, gives the greatest hope for cure.<sup>4, 9, 11</sup> Hence, it is necessary to have indisputable evidence that the lesion cannot be removed surgically before denying the patient this chance for surgical cure. Metastases to bone, brain and other organs frequently take place. If such extrathoracic extension cannot be demonstrated, evidence of local extrapulmonary involvement should be searched for. One cannot always be certain bronchoscopically that a given lesion is operable. Various findings, however, may demonstrate that extrapulmonary extension has taken place, and that the lesion is therefore inoperable. Bronchoscopy may thus save the patient a thoracic exploration.

Bronchoscopic evidence of inoperability may be grouped under two headings: local intrabronchial direct extension to an unresectable area of the tracheobronchial tree, and extensive paratracheal lymph-node involvement.

Lesions originating in either the main-stem or the right upper-lobe bronchus may extend so as to invade the wall of the nearby trachea. Such

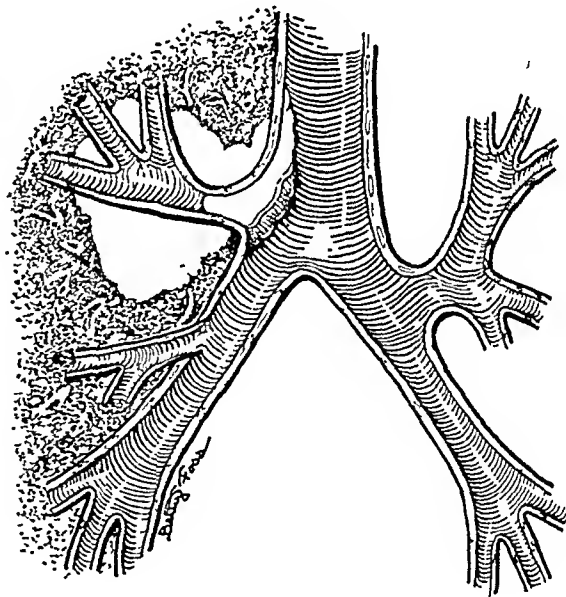


FIGURE 3.

*This drawing illustrates how a lesion originating in the vicinity of the upper-lobe orifice may, by direct extension, invade the nearby trachea and become unresectable.*

an extension can be visualized bronchoscopically and inoperability determined (Fig. 3). A not infrequent finding is involvement of the contralateral main-stem bronchus. This appears to take place by extension from the infracarinal lymph nodes (Fig. 4).

The lymphatic drainage of the lung is primarily

centripetal. When an extrapulmonary lymphatic extension takes place, the paratracheal lymph nodes are usually the first to be involved. Such involvement, if extensive, causes the angle between the two main stem bronchi to become more obtuse

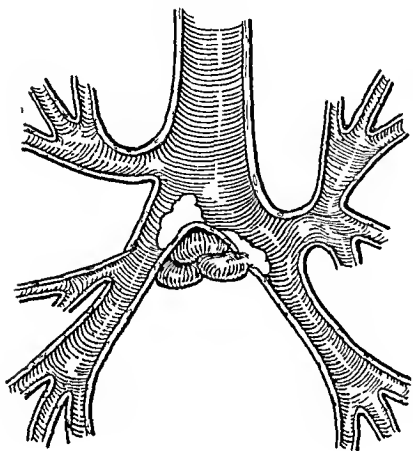


FIGURE 4

*This drawing illustrates extension to the contralateral bronchus by direct extension from a paratracheal lymph node*

Fixation may be present, just as a so called frozen pelvis is found in advanced cases of carcinoma of the cervix. The extent of mediastinal fixation can be determined by palpating these structures with the tip of the bronchoscope. The finding of a widened carina with hardened and fixed structures, as determined bronchoscopically, is prima facie evidence of mediastinal metastases, especially if a positive biopsy from the primary site has been obtained (Fig 5).

**Therapeutic value of bronchoscopy.** The usefulness of bronchoscopy is not confined to diagnosis or determination of proper treatment. It may be of therapeutic value itself. Frequently, the bronchial obstruction produced by a neoplasm causes an infectious process in the segment of lung supplied by that bronchus. Gentle bronchoscopic dilatation or even removal of a portion of the tumor mass provides better drainage and may give relief from the septic process. Repeated bronchoscopic aspirations are occasionally indicated in such cases to improve the patient's general condition preoperatively. In certain cases not amenable to surgery, radium or radon may be used in an intrabronchial applicator introduced

bronchoscopically. This procedure has been recommended as a means of destroying the intrabronchial portion of the tumor to provide drainage for the outlying pulmonary parenchyma. My experience with this type of treatment is too meager to permit drawing conclusions.

#### BRONCHOSCOPIC RESULTS

Of 62 patients\* with histologically verified pulmonary tumors examined bronchoscopically, 49 were men and 13 women, a ratio of 4:1. Their ages ranged from eighteen to sixty-seven years, with an average of fifty-two years.

The tumor originated in one of the major bronchi in 46 patients, and was more peripherally located in 16. In 46 patients (74 per cent)—45 (98 per cent) with central tumors and 1 (6 per cent) with a peripheral tumor—a biopsy and subsequent histologic diagnosis of neoplasm were obtained. The patient with a central tumor in whom a biopsy was not obtained had an inoperable lesion originating in the left upper lobe bronchus (determined at autopsy). At the time of bronchoscopy, there was so much fixation of the mediastinal structures that the bronchoscope could not be introduced as far as the upper lobe orifice, therefore, tissue was not obtained by bronchoscopy in this particular case, although a clinical diagnosis of inoperable bronchiogenic carcinoma was established.

#### Location of Tumor

The frequency of involvement of each bronchus in the series of 46 central tumors was as follows: right upper, 10; right main stem, 10; right lower, 9; left lower, 7; left main stem, 5; left upper, 3; and right middle, 2.

Thirty-one, or 67 per cent, originated on the right side, and 15, or 33 per cent, on the left. Inasmuch as satisfactory closure of the bronchus is technically the most difficult part of a pulmonary resection, it is unfortunate that the region of the right upper lobe bronchus is most frequently involved. This bronchus arises from the right main stem bronchus, from 15 to 20 cm from the trachea. A growth originating in this area may early invade the wall of the neighboring trachea and thereby become technically unresectable (Fig 3).

Malignant tumors should be removed with a margin of uninvolved tissue and all available lymphatics, since extension is most frequently by this route. The treatment of pulmonary cancer is comparable to that of cancer of the breast. And

\*Some of these patients have been previously reported by Ochsolt and Ramey.<sup>1</sup> Only patients whom I have personally bronchoscoped are included in this report.

lary dissection and resection of the lymph nodes are a part of the standard operation for breast neoplasms. For the same reason, pneumonectomy, or removal of the entire organ, is gaining precedence over lobectomy in the treatment of pulmonary cancer. Certain benign tumors, including the so-called "benign adenomas," may be treated by subtotal pulmonary resection. Inspection of the tumor mass bronchoscopically and an actual measurement of the relative position of the tumor in respect to uninvolved bronchi is the best guide to the proper level of resection. Growths

Of the 45 patients who had visible endobronchial tumors on bronchoscopy, 8 presented this type of intrabronchial propagating mass. Of these, 5 tumors were found to be resectable at operation, and 4 of the 5 patients are living and well at the present time. One died suddenly, eight weeks postoperatively, after returning home. No post-mortem examination was made, but clinically he had no evidence of metastatic disease. The relatively benign course of this group of 8 patients is further illustrated by the other 3, who were not resected. One had a lesion involving the

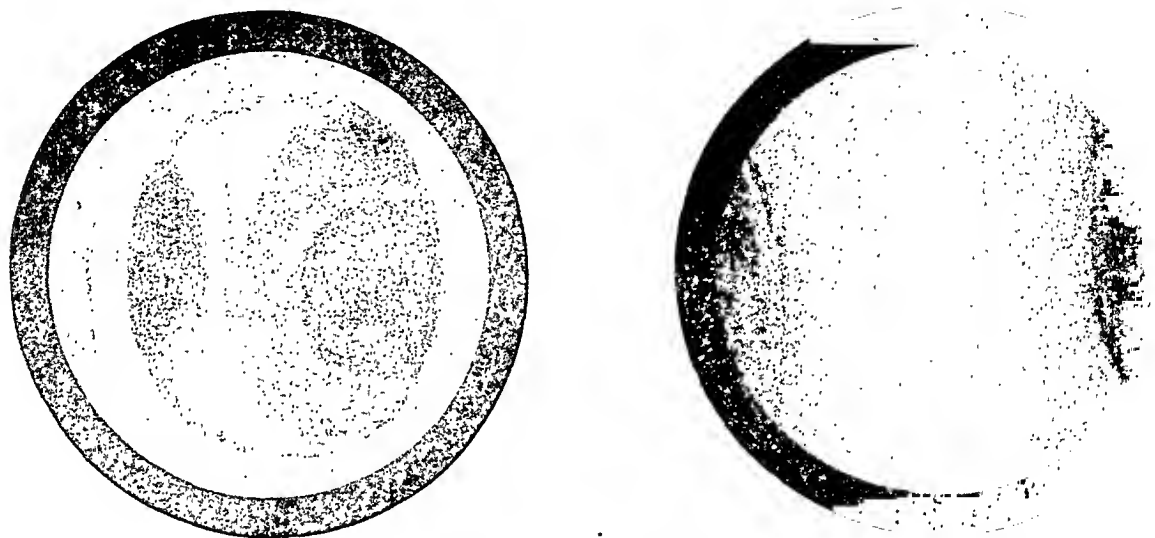


FIGURE 5. Drawings of Normal and Widened Carinas.

*Note the narrow carina on the left, compared with the widened one on the right. The angle formed by the latter is obtuse, owing to spreading of the two main-stem bronchi by a mass of metastatic infracarinal lymph nodes. On palpating the normal carina with the tip of the bronchoscope, it is flexible and quite movable. A carina such as that illustrated on the right is hard and fixed.*

usually invade the wall of the bronchus above the point of obstruction as shown by roentgenography. Thus, it will be found in most cases that a larger rather than a smaller portion of the lung needs to be removed to excise the tumor completely.

#### Gross Pathology

Various configurations are assumed by the intrabronchial portion of pulmonary tumors. Practically all consist of both an intrabronchial and an extrabronchial segment. The semirigid cartilaginous bronchial wall undoubtedly plays a role in the configuration presented. The gross appearance of the tumor has not been found to be an accurate guide to its histologic classification, except that those tumors that are pedunculated and tend to form sessile bodies within the bronchial lumen are apt to be of low-grade malignancy, and therefore particularly suitable for surgical therapy.

carina when first bronchoscoped. This patient died twenty-five months after the onset of symptoms—about twice the average length of survival. The other 2 were explored but not resected, since involved mediastinal lymph nodes were found. One died fourteen months after onset, whereas the other is still living and in comparative good health, three years and five months after the onset of symptoms and over three years since exploration. Of the other 37 patients, there was only 1 who did not have metastases, either clinically or at exploration.

#### Histology

The histology of pulmonary tumors is under a great deal of discussion at the present time, and it is known that some tumors may show varying histologic patterns in different portions of the same tumor. However, the histologic classification of the biopsy specimen from a bronchus is not so important as the determination of whether



or not one is dealing with a malignant lesion. Bronchoscopic biopsy specimens are usually small, and the pathologist is not always able to classify them according to type or grade of malignancy. A diagnosis of malignancy, however, provides a satisfactory working basis on which to plan treatment.

In this series of 47 cases with positive biopsies, the pathologist in 17 cases simply made a diagnosis of carcinoma without any attempt at classification from the biopsy specimen. The others were classified as epidermoid carcinoma in 20, adenocarcinoma in 3, carcinoma simplex in 4, undifferentiated or oat-cell carcinoma in 1 and benign adenoma in 2. In 18 cases in which subsequent surgical procedures or autopsy examination provided the whole specimen, the final diagnosis was the same as the biopsy in 9, or 50 per cent.

Owing to the lack of knowledge of the histopathology of lung tumors in general and the inability to classify the tumor accurately from the biopsy specimen, it seems that for the present the treatment of all carcinomas of the lung should be the same regardless of the histology of the tumor, as revealed by bronchoscopic biopsy.

#### SUMMARY AND CONCLUSIONS

Evidence points to an increase in incidence of cancer of the lung. Approximately 10 per cent of all deaths ascribed to cancer are due to primary lung tumors.

The symptomatology and physiologic disturbances in primary lung tumors are so bizarre and apparently confusing that only a complete investigation, including bronchoscopic study, provides

a satisfactory basis for the determination of therapy.

Bronchoscopy is an easily performed diagnostic procedure without risk to the patient. It should be considered in every case of unexplained pulmonary symptoms.

A series of 62 verified pulmonary tumors is presented. In this group, the diagnosis was established by bronchoscopic biopsy in 46 cases, or 74 per cent.

Primary cancer of the lung should be favorable for surgical treatment in view of the high percentage of positive preoperative biopsies and the ability to make an early diagnosis by bronchoscopic means.

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## AUSCULTATION OF THE HEART\*

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BOSTON

The hearing ear, and the seeing eye,  
The Lord hath made even both of them.

*Proverbs XX: 12.*

AUSCULTATION of the heart is only one of the many methods available for the study of cardiac function and for the detection of cardiac disease. Although it is well for teachers to exhort their students to learn as much as possible by other means, such as the history of the patient, inspection, palpation and percussion, there is no reason to minimize the importance of auscultation or to fail to elicit all possible aid from such a simple procedure. For among all the simple heart findings that one can make, the auscultatory observations are unique and may be regarded as *sui generis*. They cannot easily be confused with those due to other neighboring organs. Furthermore, the use of the stethoscope is easily mastered, and the instrument is available to every physician. In the present era when the economic aspect of the care of the sick is so pressing a matter, any data that can be obtained quickly and without additional cost to the patient are valuable. Moreover, there is certain information that can be obtained only by auscultation.

In performing proper auscultation, one must know what is to be heard. Gross objects are easily seen; minute findings are detected only if one searches carefully. A large goiter cannot escape detection, but a small tophus must be deliberately looked for. Likewise, a loud murmur will not be overlooked, but a telltale gallop rhythm will be heard only by the knowing ear. In a word, one must not only understand how to interpret what one hears but must also be familiar with the various possible peculiar abnormalities that are detectable by auscultation, paying particular attention to different phenomena under different circumstances. The same principle is true throughout medical practice. If a patient's primary complaint is pain in the right loin, which radiates into the groin, one should naturally search for blood in the urine, thinking of a renal calculus. Certainly one would not spend much time looking for a systolic thrill at the base of the heart. On the other hand, if a patient has attacks of syn-

cope and there is a loud systolic murmur over the aortic area, knowing that both might be explained by the presence of aortic stenosis, one should spend a few moments, if necessary, to elicit a systolic thrill, even palpating the chest with the patient sitting up and holding a deep expiration. It is the thoughtful choice of the necessary procedures that spells success in medicine, for no physician can afford to make a so-called "complete" physical examination every time he sees a patient.

Among the various objectives in carrying out intelligent auscultation, the interpretation of the irregularities of the heart is most important. As a result of intensive study and the aid that has come from modern electrocardiography, most of the disturbances in the mechanism of the heart beat can now be detected by simple auscultation. It is a general axiom that the more thoroughly one understands electrocardiography the less one needs it. For this reason alone, it is well for students and practitioners to become familiar with this subject. It is needless in this discussion to take up all the arrhythmias, but I do want to mention some useful points in diagnosis that illustrate how sensitive the ear may be in drawing very fine conclusions from minute auscultatory abnormalities.

When the rhythm of the heart is found to be regular and the rate within normal range, one can usually assume that the mechanism is normal. Like all generalities in medicine, even this has its exceptions. If one had reason to suspect that the mechanism of the heart was disturbed, one might be led to look for some condition like auricular flutter. I recall seeing a young man who complained of palpitation. He appeared to be in good health and showed nothing abnormal on examination. The heart was regular and showed no murmur or enlargement, and the rate was 70. Directly after taking twenty-five hops, the rate was exactly 140 and perfectly regular for a minute or two, following which the rhythm became irregular and gradually returned to the previous level of 70 in a jerky fashion (Fig. 1). This simple observation led to the conclusion that the patient had auricular flutter, that the auricles were beating at a rate of 280, that at first there was a regular 4:1 block with a regular ventricular rate of 70, and that with exercise the block suddenly

\*The Frank N. Wilson Lecture in Cardiology, given at Ann Arbor, Michigan, November 19, 1940.

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changed to 2:1, resulting in a regular rate of 140. It would otherwise be difficult to explain the exact doubling of the ventricular rate on effort. One might expect the rate to rise to 96, 119 or some other odd figure if the mechanism were normal. Furthermore, a normal heart would accelerate and retard gradually and smoothly following effort and would not become irregular. This simple observation illustrates how detailed a conclusion can be drawn by intelligent auscultation.

The following is another exception in which one

### AURICULAR FLUTTER

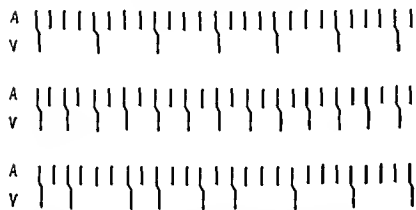


FIGURE 1 Response to Effort in Auricular Flutter

*The upper lines indicate the auricular contractions (inaudible), at a rate of 280 throughout the lower lines represent the ventricular responses (audible heart rate). The first set shows a regular ventricular rate of 70; the second set, directly after brief effort, shows a regular ventricular rate of 110; the third set—a continuation of the second—shows irregular slowing to the original slow regular rate of 70.*

might suspect an abnormal mechanism despite a regular normal heart rate. A forty-five-year-old woman, who had had rheumatic fever in childhood, was known to have had mitral stenosis and auricular fibrillation with a grossly irregular heart beat. She had been taking digitalis for some time, and on this particular occasion it was noted that the heart rate was 60 and perfectly regular. The question that came up was whether the auricular fibrillation had changed to normal rhythm. An early apical rumbling diastolic murmur was heard, quite typical of mitral stenosis. On careful auscultation, no murmur whatever could be detected in presystole. This led to the suspicion that auricular fibrillation was still present and that the regular ventricular rate was due to so-called 'digitalis complete heart block'. This suspicion was warranted, because in most cases of mitral stenosis a presystolic murmur is heard if the auricles are contracting and is absent if they are fibrillating.

When the rhythm of the heart is not regular, it is incumbent on the examiner to try to identify the exact type of irregularity. The time has passed

when a physician should be content with the vague observation that the heart is 'slightly irregular' or 'more or less irregular' without trying to determine the type of irregularity. It is just as inadequate an observation as to say that a patient has more or less fever without determining whether it is due to typhoid fever, tuberculosis or pneumonia. A slight irregularity might be the sole clue to a diagnosis, and might lead to correct and effective therapy.

Extrasystoles are very common, occurring both with and without organic heart disease. Owing to the premature contraction of the heart, one hears a quick beat, which may or may not reach the wrist, followed by an abnormally long pause. If the extrasystole is ventricular in origin, this pause is apt to be completely compensatory so that the dominant rhythm is not disturbed, if it is auricular, the pause is not quite so long. This differentiation is not invariable, nor is it a simple matter for the ear to make this distinction. Occasionally it may be useful during auscultation to tap with one's foot in rhythm with the regular beat, not changing the pace, to see if the tap comes exactly on time or after the first beat following the pause. There is another auscultatory finding, however, that may help in distinguishing an auricular from a ventricular extrasystole. An auricular extrasystole sounds a good deal like a normal beat but is heard prematurely. The first heart sound of a ventricular extrasystole has an abnormal clicking quality. The reason for this difference in quality between the two types of premature beats is that the relation between auricular and ventricular systole is different. In the auricular, the normal sequence of auricular and ventricular contraction occurs, whereas in the other the ventricles contract before the auricles. Inasmuch as the position of the auriculoventricular valves at the moment of ventricular contraction greatly influences the quality of the heart sound, one can see that the character of the first heart sound may differ perceptibly in the two types of extrasystoles.

One may ask whether it is of any value to distinguish the various types of premature beats. Generally it is of no great moment, but occasionally it can help in identifying types of paroxysmal rapid heart action. These paroxysms come and go, and the physician may find it difficult to observe the patient while the attack is on. The finding of ventricular extrasystoles during the interparoxysmal periods may point to attacks of ventricular origin, whereas auricular extrasystoles may indicate attacks of auricular origin. Obviously prognosis and treatment may be quite different in the two conditions.

The diagnosis of auricular flutter is generally

very difficult without electrocardiographic aid. In many cases, however, with increasing experience and study, it has become possible to make accurate bedside diagnoses by auscultation. One simple point briefly mentioned above deserves further emphasis. It should be recalled that the sounds result mainly from ventricular contraction. One thereby infers what the auricles are doing. In flutter, the auricles are contracting very rapidly, perfectly regularly and inaudibly. The audible ventricular rate is slower, and may be regular or irregular. When it is regular, the rate must be a simple fraction of the auricular rate (except for the rare cases in which there is a 1:1 response). This means that if the heart rate is 140 the auricular rate must be 280. It cannot be 265 or 311 or any other figure. If the regular ventricular rate is 168, the auricular rate must be 336. Hence, realizing that the auricular rate in an untreated case of flutter is hardly ever under 200 or over 360 and that there is practically always an accompanying heart block, one can draw some simple conclusions. If a regular heart rate is about 198, it cannot be due to flutter, for the auricular rate would have to be 396, which is too rapid or 198, which is too slow. The same reasoning applies to ventricular rates around 210 to 230.

There is another peculiarity that is quite characteristic of auricular flutter. When the mechanism of a regular rapid heart is unknown, vagal

return of the rapid rate, one can be quite sure that it is not a paroxysm of auricular tachycardia, but there is still doubt whether it is a normal sinus tachycardia or auricular flutter. If careful attention is paid to the way in which the previously rapid rate is resumed after the temporary slowing takes place, this differentiation can be made (Fig. 2). In normal sinus tachycardia, the process is smooth and gradual, each beat becoming faster and faster until the original rapid rate returns. In flutter, on the other hand, the recovery of the tachycardia occurs in an irregular or jerky fashion. After the temporary pause or slowing, one or two quick beats may occur, then a slow beat, another quicker beat followed by a somewhat slower one,

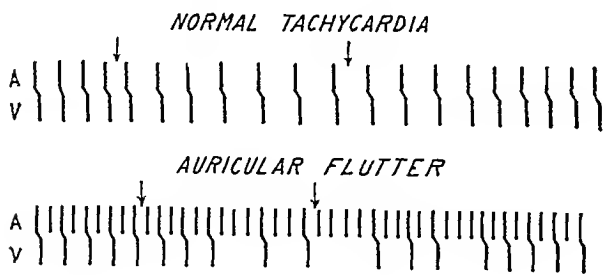


FIGURE 2. Response to Carotid-Sinus Pressure. A represents the auricular beats; V, the ventricular beats. The arrows indicate the duration of carotid-sinus pressure. The upper tracing shows gradual slowing from vagal stimulation and a smooth return to the fast rate in a case of normal tachycardia. The lower drawing shows sudden slowing and a jerky return to the original fast rate in a case of auricular flutter. Both started and ended with a regular rate of about 150.

slowing by carotid-sinus pressure may help to reveal the underlying disturbance. Everyone knows that if the attack is abruptly stopped by such a procedure the condition must have been a paroxysm of auricular tachycardia, for no other mechanism will respond in such a fashion. However, if there is temporary slowing with prompt grad-

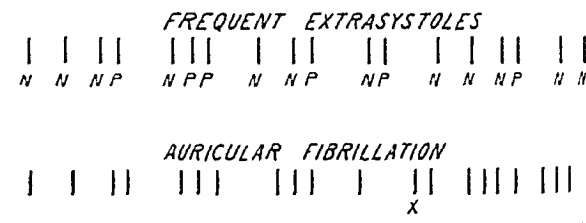


FIGURE 3. Difference between Frequent Extrasystoles and Auricular Fibrillation.

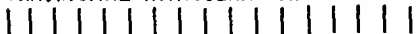
The upper drawing shows many premature beats (P) preceded by normal beats (N) and followed by compensatory pauses. The lower drawing, which superficially resembles the upper, also shows quick and slow beats, but at one point (X) a slow beat is not preceded by a quick beat. This typifies auricular fibrillation.

until finally the original rapid regular rhythm is resumed. These irregular beats are heard because while the auricles have been very rapid, regular and entirely undisturbed by the vagal stimulation, the degree of auriculoventricular block has been varying. Similar observations may be made if the patient can hold a deep breath or is asked to perform some brief effort. These minute auscultatory changes enable the physician to draw very accurate observations at the bedside.

After a certain amount of training and experience, the diagnosis of auricular fibrillation by auscultation in most cases becomes a fairly simple matter. Occasionally difficulties arise, for it may be confused with auricular flutter when there is a changing degree of block, with frequent extrasystoles or other less common combinations of arrhythmias. In some cases, there is no way of establishing a certain diagnosis without electrocardiographic study. Frequently, however, when confusion arises, correct decisions can be made by the use of simple methods. When for one reason or another the possibility of auricular flutter arises, accelerating the heart rate by having the patient bend up and down in bed several times will give

the answer. In flutter, the rate is apt to become rapid and perfectly regular for a short while, and in fibrillation the gross irregularity will persist. What is more difficult is to distinguish frequent and multiple extrasystoles from auricular fibrillation. Both conditions may have short and long pauses between beats. There may be short runs

#### PAROXYSMAL AURICULAR TACHYCARDIA



#### PAROXYSMAL VENTRICULAR TACHYCARDIA



FIGURE 4. Difference between Paroxysmal Auricular and Paroxysmal Ventricular Tachycardia

The upper drawing shows perfectly regular beats in a case of paroxysmal auricular tachycardia, at a rate of 180. The lower drawing shows slight but definite irregularities in a case of paroxysmal ventricular tachycardia, at the same rate.

of quick beats followed by pauses when there are two or more extrasystoles in quick succession or when they are interpolated. Both may have an appreciable pulse deficit, and may appear to present a total irregularity of the heart. The finding that identifies the arrhythmia as auricular fibrillation is the occurrence of a pause not preceded by a quick beat (Fig. 3). A sudden lengthening of the cycle that follows a quick beat may be due to a compensatory pause after an extrasystole or

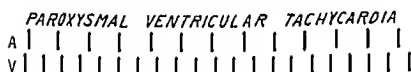


FIGURE 5. Changing Quality of Sounds in Ventricular Tachycardia.

The upper lines represent auricular contractions, at a rate of 113; the lower, the ventricular contractions, at a rate of 190. Note the changing time relation between the auricular and ventricular contractions; this changes the quality of the first heart sound.

to fibrillation, but a sudden pause following a beat of normal length will for the most part be due only to auricular fibrillation. After hearing such a sudden lengthening of the heart cycle, one must think back and recollect whether or not the previous cycle was short.

There are characteristic auscultatory findings in most cases of ventricular tachycardia, one of the uncommon but very important cardiac arrhythmias. Unlike paroxysmal auricular tachycardia,

in which the heart beat is almost invariably perfectly regular and the consecutive sounds of identical character, this disturbance is frequently slightly irregular and there may be slight but definite alterations in the intensity or quality of the first heart sound (Figs. 4 and 5). For ten or more beats, the rhythm may be perfectly regular and the heart sounds quite similar in character, just as in auricular tachycardia, and then suddenly for two or three cycles slight but detectable irregularities appear both in time and in the quality of the beats. This peculiarity is due to the changing relation between auricular and ventricular systole that takes place in many cases of ventricular tachycardia; this relation is constant in auricular tachycardia. On rare occasions, I have detected this peculiar alteration in the quality of the heart sounds even when the ventricular rate was perfectly regular, because the auricles were contracting independently and at a different rate. These detailed observations can be made at the bedside by any well-trained physician and may enable him to arrive at a quick decision and institute proper treatment. From a therapeutic point of view, the decision may be a matter of life and death, for ventricular tachycardia generally responds favorably to quinidine therapy and is refractory or aggravated by digitalis.

The diagnosis of the different degrees of heart block can often be recognized by auscultations. In first-degree heart block (simple delayed PR interval), the rhythm of the heart is perfectly regular. This disturbance, therefore, is generally overlooked, unless graphic registration of the heart beat is employed. However, if there is some reason to suspect its presence, as during rheumatic fever, the detection of a definite diminution in the intensity of the first heart sound at the apex points more strongly to this diagnosis. This is particularly true if the intensity of the first heart sound is observed to diminish during the illness. The reversal of this process can also be followed, that is, the gradual return of the previous normal intensity of the first heart sound as the patient is recovering and the conduction time is becoming normal. The reason for the above phenomenon is that the loudness of the first sound is directly related to the PR interval. It is loudest when it is between 0.04 and 0.10 second, normal in intensity between 0.12 and 0.16 second, and gradually becomes fainter when it is 0.20 to 0.28 second or longer. These differences, as mentioned above, probably result because the mitral and tricuspid valves are caught in different positions at the moment of ventricular systole, depending on the time the auricles contract.

Occasionally, in first-degree heart block, one may hear a third heart sound in diastole, resulting in what sounds like a gallop rhythm. This is probably in some way related to the early contraction of the auricle. When it is present and the commoner causes of gallop rhythm, such as hypertensive heart disease and coronary-artery disease, can be satisfactorily dismissed from consideration, it should make one suspect delayed conduction time. These auscultatory findings are of particular importance because there are no other simple means of detecting this condition, and the fact that the heart is perfectly regular otherwise makes the physician entirely oblivious to

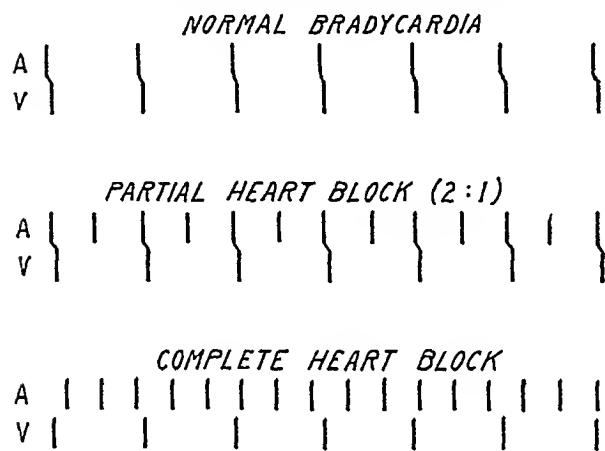


FIGURE 6. Bradycardia.

The first drawing (normal bradycardia) shows auricles and ventricles beating slowly and regularly, at a rate of 35. The second (2:1 heart block) shows an auricular rate of 70 and a ventricular rate of 35. The third (complete heart block) shows an auricular rate of 93 and a ventricular rate of 35. In all, there is a regular ventricular rate of 35, but only in the last is there a changing quality of the first heart sound, because of changing relation between the auricular and ventricular systoles.

any disturbance of the mechanism of the heart beat.

Second-degree or partial heart block (dropped beats) is readily recognized because the loss of an entire heart cycle is easily heard on auscultation. It must not be expected that the pause will be quite so long as two normal heart cycles, because the last beat before the pause is accompanied by a long PR interval and the one after the pause by a much shorter PR interval. In sinoauricular block, a far rarer condition, this pause is much likelier to be exactly equal to two heart cycles. Partial heart block must not be confused with extrasystoles. In both, the peripheral pulse may intermit for an entire cycle, but with extrasystoles a premature beat ought to be heard over the precordium during this interval, and in block

no such beat will be present. The difficulty is that premature beats are very rarely inaudible and in auriculoventricular block a faint auricular sound may resemble an extrasystole. In these cases, one is entirely dependent on electrocardiography.

There is one auscultatory sign that is quite pathognomonic of complete heart block. Apart from the slow, generally regular beat of 30 to 40, one should pay particular attention to the quality of the first heart sound in different cycles. If the heart is slow at a rate of about 35 to 40 and regular, it can be due to complete block, to a regularly recurring 2:1 block or even to a normal bradycardia (Fig. 6). In the last, there may even be no heart disease whatever. The differentiation between these conditions may therefore be quite important: If there is complete dissociation (except for the rare cases in which auricular fibrillation is also present), the first heart sound varies in intensity or quality in different cycles, sometimes suddenly becoming booming or muffled or reduplicated. Just as in ventricular tachycardia, this is owing to the changing relation between the time of auricular and ventricular systole. When the slow rate is due to 2:1 block or to a normal bradycardia, the sounds are all alike. It must be borne in mind that hearing auricular beats during the long ventricular pauses, although a common finding in heart block, does not mean that the block is complete. It is the peculiarity of the first heart sound above mentioned that identifies the condition as complete dissociation.

Apart from the irregularities of the heart, the quality of the sounds may have significance. Distant heart sounds need not indicate heart disease, since they often result from pulmonary emphysema or a thick chest wall. In the absence of these or other obvious causes, and especially if the heart sounds are known to have been of normal intensity shortly before, a marked diminution in the intensity of both heart sounds occurs in some cases of acute coronary thrombosis and in extensive pericardial effusion. Apart from these considerations, so-called "weak heart sounds" have little clinical value. The term is often misleading, for the connotation that the heart is weak need not be true.

Accentuation of the first heart sound may have considerable diagnostic value. It is frequently an early evidence of developing mitral stenosis and should lead the examiner to search with greater care for the short presystolic or mid-diastolic murmur that characterizes mitral stenosis. Furthermore, a snapping first heart sound may be the first clue that the patient has hyperthyroidism. It is obvious that in the classic case of thyrotoxicosis

other features, like exophthalmos, enlarged thyroid gland, a typical history of nervousness, palpitation and loss of appetite, readily reveal the true nature of the underlying morbid process. In some of the obscure cases, however, many of these points are lacking, and one may be led to the diagnosis by auscultation of the heart. Accentuation of the first heart sound may also be found in nervous patients, in hypertension, in anemia and in some fevers, especially rheumatic fever.

There is one condition that I especially wish to mention because it has only recently been recognized as a clinical entity and is one in which the first sound is also distinctly accentuated. It is the syndrome of short PR interval with curves resembling bundle-branch block occurring in patients prone to have paroxysms of rapid heart action. It was first called to attention as a clinical unit by Wolff, Parkinson and White,<sup>1</sup> although Wilson<sup>2</sup> reported an isolated case of this sort many years before. These patients, who apparently show no evidence of organic heart disease, are subject to attacks of palpitation and show an unusually short PR interval when the heart rate and rhythm are normal. The only method suggesting the presence of the abnormal mechanism before electrocardiograms are taken is the detection of an unusually accentuated first heart sound. I mention this because only recently I had such an experience, and the auscultatory suspicion was validated by electrocardiographic study.

In the diagnosis of acute pericarditis, one is almost entirely dependent on auscultation. There is nothing in the history or in other methods of examination that is so helpful diagnostically or in fact that may throw any light whatever on the diagnosis. Unless one hears the telltale to-and-fro pericardial friction rub, one is generally unable to make the diagnosis of acute pericarditis. Inasmuch as this sign is likely to be transient and may last only a day or so, frequent auscultation is necessary. Occasionally, it is heard only if the patient sits up or bends forward. Apart from its specific diagnostic value, its detection may help in identifying one illness as being rheumatic, another as acute coronary thrombosis, and so on.

Gallop rhythm is a purely auscultatory phenomenon. Although in some cases there are other associated phenomena, such as bundle-branch block, a doubling of the apex impulse and pulsus alternans, the quality of the heart sounds alone has a specific connotation. Care must be taken to differentiate a diastolic from a systolic gallop. The former almost invariably signifies grave heart dis-

ease; the latter is found in structurally normal hearts. The differentiation may be facilitated by the following procedure. When a so-called "normal" or midsystolic gallop is present, it is heard at the apex, and on rhythmically moving the stethoscope toward the base of the heart, one finds that the abnormal third sound gradually disappears. It should also be noted that the sound to disappear is the middle one of the three, leaving the two normal heart sounds that are customarily heard at the base of the heart. It is also of some clinical interest that the common diastolic gallop rhythm that generally indicates a grave prognosis is extremely rare in auricular fibrillation or flutter. Occasionally, this antagonism is indirectly helpful in diagnosis, when a gallop disappears and a new rhythm is established. Finally, a word of caution may be appropriate concerning the confusion between cases with gallop rhythm and those showing a normal third heart sound or those in which a third sound in mid-diastole proves to be the early evidence of developing mitral stenosis. Experience and mature judgment are required to make these differentiations.

Pulsus alternans is a peculiarity of the peripheral pulse in which alternate regular beats are strong and weak. It connotes grave heart-muscle disease. Not infrequently, this may be detected on auscultation of the heart itself, when the heart sounds or an accompanying systolic murmur are found to alternate in intensity.

There are other extremely rare cases in which peculiar sounds are heard over the precordium. A tinkling or splashing sound with each heart beat suggests both air and fluid in the pericardial sac or a diaphragmatic hernia with the heart pulsating against the stomach contents. Recently Hamman<sup>3</sup> described unusual crunching sounds with the heart beats in acute mediastinal emphysema, a condition that is easily confused with acute coronary thrombosis. These are all very rare conditions, but they are recognized mainly through auscultation.

Finally, the subject of cardiac murmurs must be considered. This is not the occasion to discuss the significance or interpretation of specific murmurs. I do wish to emphasize that the detection and proper interpretation of murmurs is a very important function of the clinician. It is true that the question whether a heart is failing is not dependent on the presence or absence of murmurs. Nor may the presence or absence of murmurs decide whether the symptoms of which a patient complains are due to the heart. But very often the pres-

ence or absence of murmurs determines whether there is organic heart disease. No simple method of diagnosis other than auscultation is valid in chronic valvular disease. Very often, the decision whether the heart is perfectly normal or whether there is early aortic insufficiency or mitral stenosis can be made only when a faint diastolic blow along the left sternal border or a short presystolic murmur at the apical region is heard. In some cases, the diagnosis depends entirely on these auscultatory findings, for electrocardiograms and roentgenograms may fail to reveal significant abnormalities. When it is realized that patients have compensated organic valvular disease for many more years than they have heart failure and that they often desire to know whether heart disease of any sort exists, this subject must be of considerable importance.

As a corollary of the above, it is well for physicians to develop confidence in detecting cardiac murmurs, for if one can be certain that there are no murmurs whatever it makes it extremely unlikely that there is any valvular disease. This question is of significance for patients who have recovered from rheumatic fever or chorea. When they are seen years later, the complete absence of murmurs means that the heart has entirely escaped permanent injury and they may be regarded as normal, unless a new infection later develops. While any murmur is present, although they may yet carry on normally, they are subject to the hazard of progressive stenosis of the valves and subsequent congestive failure or superimposed bacterial endocarditis. In other words, it is my opinion that apart from the acute stages of rheumatic infection, when the involvement of the heart muscle is paramount, the subsequent health of the patient depends entirely on involvement of the

valves. The development of chronic heart failure in rheumatic valvular disease is directly or indirectly the result of the mechanical insufficiency or constriction of the valves and is not dependent on any peculiarity of the heart muscle. It may be considered that the myocardium recovers completely or that at least its involvement is insignificant in determining the ultimate outcome in most patients with rheumatic heart disease who do not succumb early, during the active stage of infection. This point of view is emphasized to counteract a prevailing concept that places all importance on the myocardium in determining the development of heart failure. Although the myocardium is of primary significance in hypertensive heart disease and in coronary-artery disease, I believe that it plays a minor role in chronic rheumatic valvular disease.

There are many more valuable diagnostic points to be elicited by auscultation than I have mentioned. Some have been deliberately omitted because they are common knowledge, others because of my own limitations. There remains much that will yet be learned by further study. If I appear to have overemphasized the use of auscultation, it must be laid to my interest in this subject. It has one great advantage, however: the procedure is valuable and simple, and the data are inexpensively obtained and available to all students and practitioners. If for no other reason, it merits serious consideration.

270 Commonwealth Avenue

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# POLLEN AND MOLD SURVEY OF SOUTHEASTERN NEW ENGLAND—1940

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THERE are few reports on the seasonal contamination of the air in New England with the pollens and molds that are proved excitants of asthma and hay fever. Rackemann and Smith<sup>1</sup> Durham<sup>2-4</sup> and Pratt<sup>5-6</sup> have each recorded pollen or mold surveys from single stations in Boston. Sylvester and Durham<sup>7</sup> have presented a relatively complete study of the ragweed season in Maine, demonstrating the diminishing amount of ragweed pollen found in the air as one progresses north from Portland. In view of the paucity of such reports, it was considered advisable to make a more thorough co-operative study, with special reference to the variation of daily counts from adjacent stations within the City of Boston and to compare these with counts at Worcester, Providence and suburban Boston.

## METHOD

Six stations were established, brief descriptions of which follow:

**Station 1 Boston** The roof of the five story main building of the Children's Hospital, Longwood Avenue, exposed to the wind from all directions.

**Station 2 Boston** A third floor window frame at the Beth Israel Hospital, Brookline Avenue, exposed to the wind from the northeast, east and southeast.

**Station 3 Boston** The roof of the five story Lahey Clinic building on Commonwealth Avenue, exposed to the wind from all directions but especially from the east and west.

**Station 4 Newton Center** Six inches above the ground, 25 feet from a house in a suburban district where the houses are 50 to 100 feet from each other, exposed to the wind from all directions, but especially from the southwest, southeast and northwest.

**Station 5 Providence, Rhode Island** A second story porch in the residential district exposed to the wind from the northeast, east, southeast and south.

**Station 6 Worcester, Massachusetts** The roof of the three story Memorial Hospital in a thickly settled district, exposed to the wind from all directions.

Stations 1, 2 and 3 are on the western edge of Boston and within a mile of each other. The area is characterized by apartment houses, vacant lots and shade trees.

At each of the six stations, slides were exposed under a cover 2 to 3 feet square and 6 to 8 inches above the slide. The slides were open to the weather. Between 8 and 9 o'clock each morning, a slide coated with glycerin jelly was exposed at each station and collected twenty four hours later. Over week ends and on holidays, slides were exposed for forty eight hours. The pollen grains and *Alternaria* spores falling on 18 square centimeters were identified and counted. The slides were stained with Calberla's fluid to assist in identification of the pollen grains. In addition, the number of colonies of *Alternaria* growing on a thin layer of Sabouraud's medium in Petri dishes exposed to the outside air for a half hour three times weekly was determined. Taking into account time and area, the slide counts should theoretically be about 40 per cent higher than the plate counts.

Charts were constructed in which the number of pollen grains or *Alternaria* spores falling on 18 square centimeters in twenty four hours is represented as the ordinate and the dates as the abscissa. Where slides were exposed for forty eight hours, the counts were divided by two and charted as if for individual days.

## RESULTS AND COMMENT

Figures 1, 2, 3 and 4 represent the pollen counts for the average of the three Boston stations and for Newton Center, Worcester and Providence respectively. All show the same variations with fairly well demarcated tree, grass and weed seasons. Table I itemizes the actual dates when appreciable amounts of pollen were in the air at each station for the 1940 season. It will be observed that the dates are remarkably similar for each station except for the end of the grass season, which terminated gradually during July. The weed pollens stopped abruptly with frost on September 24.

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A comparison of Figure 1 for the Boston stations and Figure 2 for Newton Center demonstrates the difference between city and suburban

weed pollens were much more abundant in the suburban area.

Figure 5 represents the pollen counts at two

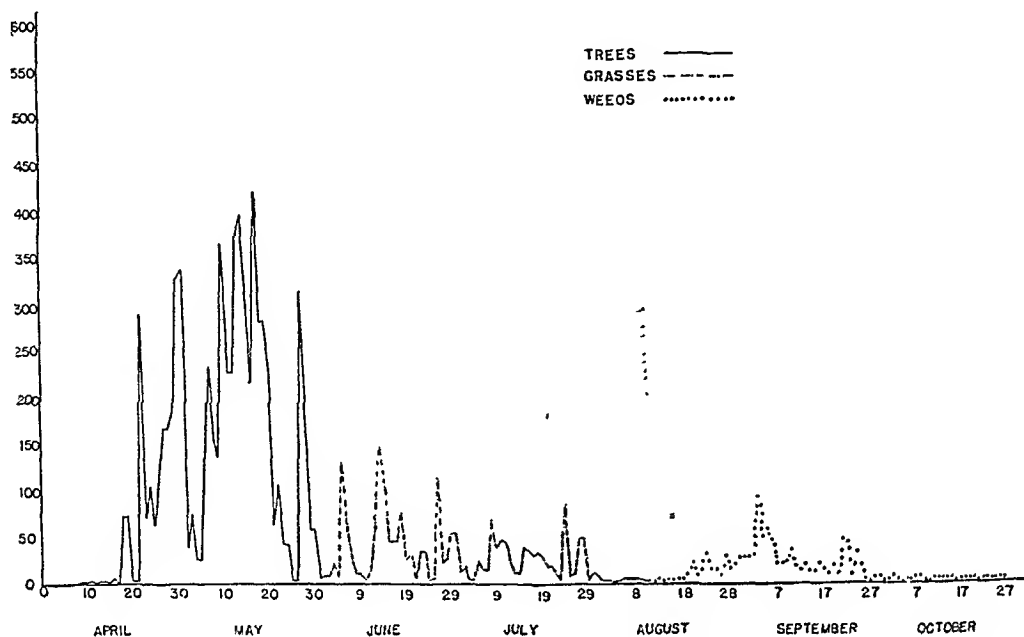


FIGURE 1. Average Pollen Counts at Three Boston Stations.

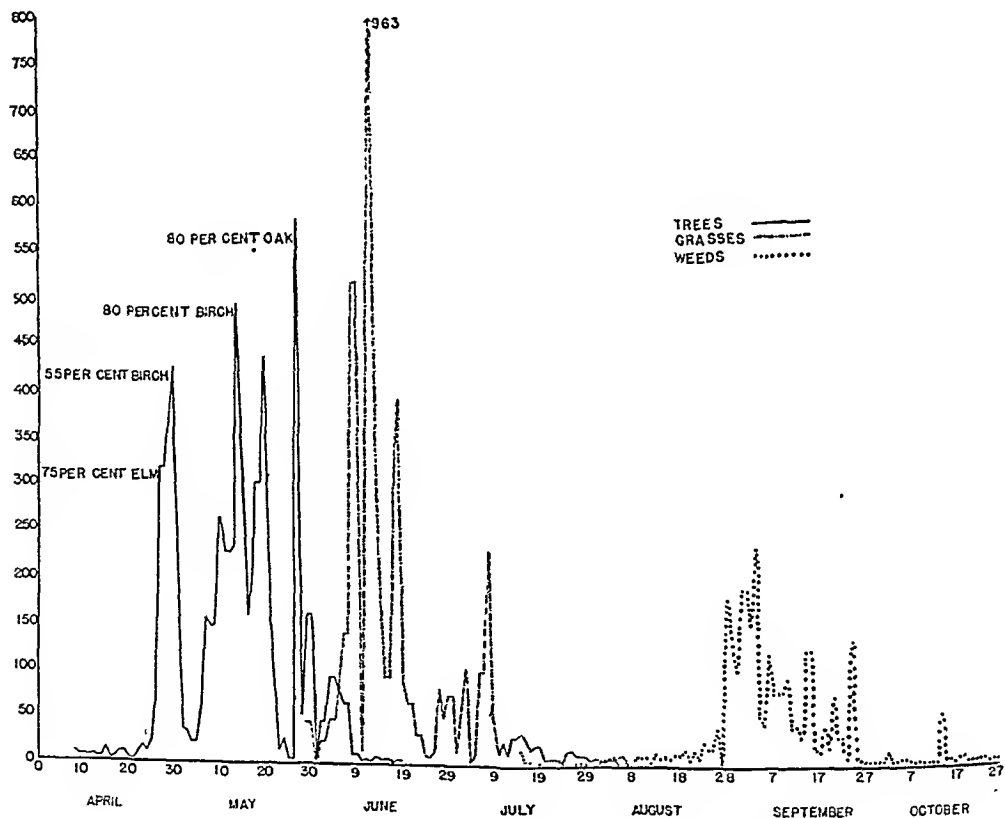


FIGURE 2. Average Pollen Counts at Newton Center.

areas. In both places, the tree counts are of the same order of magnitude, because shade trees are numerous in the parts of the city studied. However, it is not surprising to find that grass and

Boston stations only a few hundred yards apart. Failure of the pollen peaks to be consistently superimposed demonstrates that local variations in vegetation and wind currents may grossly affect

the counts. This suggests one reason why all hay-fever patients do not have severe symptoms on the same days.

and asthma, and yet when pollen counts are made by the gravity method, the weeds appear to be the least important, if quantity is any criterion.

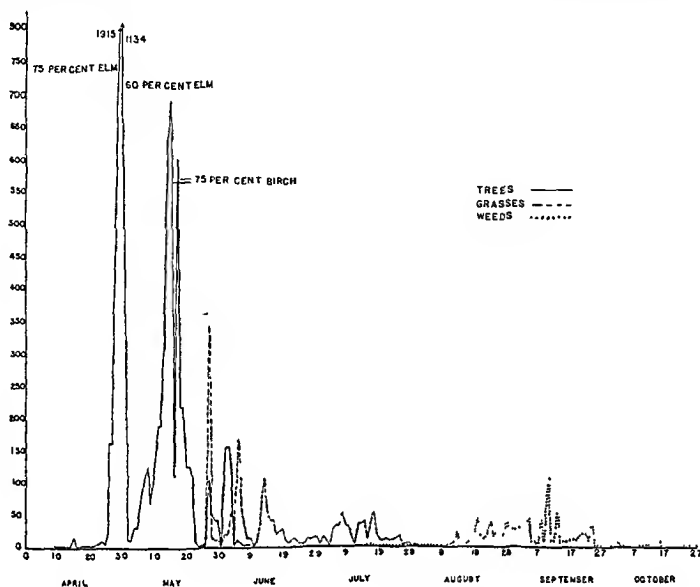


FIGURE 3 Average Pollen Counts at Worcester.

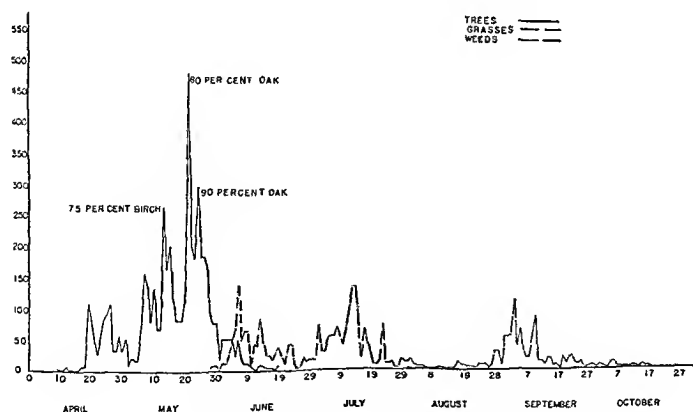


FIGURE 4 Average Pollen Counts at Providence.

It has been recognized from clinical evidence that the weed pollens from late August to frost are the commonest seasonal excitants of hay fever

This paradox is explained when the number of pollen grains per cubic yard of air is calculated. Stokes's law for falling bodies, as adapted by

Scheppegregg<sup>8</sup> and corrected by Cocke,<sup>9</sup> has been experimentally shown by Cocke<sup>10</sup> to be accurate for pollen grains if the spiculated surface of the weed pollens is taken into account. Utilizing Cocke's tables and assuming that Wodehouse's<sup>11</sup> figures for pollen size are correct, the average number

fore probably the most important clinically. There were moderate amounts of poplar and maple pollen and a little alder, ash and beech. Pine pollen frequently appeared on the slides in fairly large amounts, but since pine pollen contains no atopic excitant,<sup>12</sup> it was omitted from the charts

TABLE 1. Pollens During 1940 Season.

STATION	TREES	GRASSES	WEEDS
Three Boston stations	April 22-May 27	June 5-late July	August 20-September 24
Newton Center	April 27-May 30	June 6-July 8	August 26-September 24
Worcester	April 26-May 22	May 27-late July	August 19-September 24
Providence .	April 19-May 28	June 5-July 23	August 28-September 10

of pollen grains per cubic yard of air for each day was calculated for Newton Center and is shown in Figure 6. Because of its small size and spiculated surface, the ragweed granule settles out of the air much more slowly than the larger, smooth, tree and grass grains. Figure 6 gives a clearer

and calculations. At two stations where linden trees were in the neighborhood, a small quantity of pollen was recovered in July, but linden is a flowering tree and is not generally considered to be a cause of hay fever or asthma.<sup>11</sup> It, too, was omitted from the charts. Occasional grains of

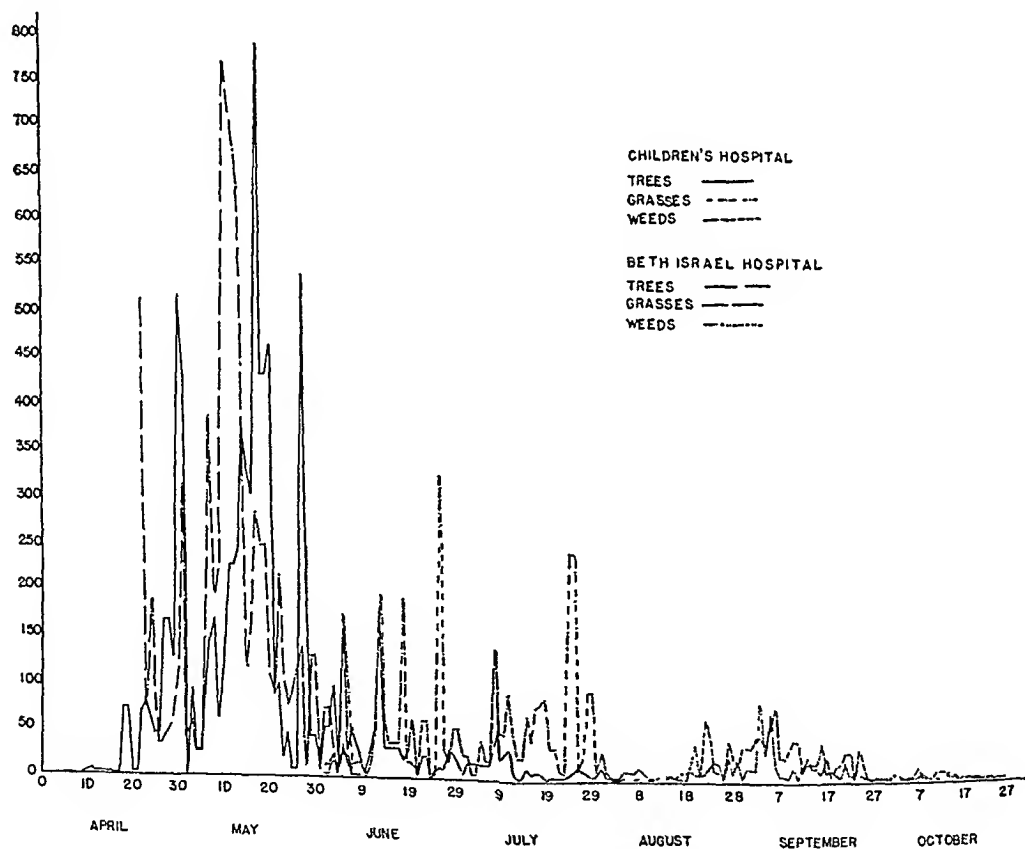


FIGURE 5. Average Pollen Counts at Two Boston Stations.

picture of the clinical significance of the three pollen seasons. Taking thirty-one consecutive days in each of the three seasons and calculating the average contamination of the air per cubic yard for this period for each season, the results are: trees 415, grasses 250 and weeds 555.

Among the trees, elm, birch and oak were by far the most abundant pollinators and are there-

unidentified pollen were also disregarded.

There are five common grasses in New England: June, orchard, sweet vernal, red top and timothy. The pollens of these grasses and of plantain are very difficult to differentiate, and therefore no effort was made to separate them. Furthermore Rackemann and Wagner<sup>13</sup> have shown by desensitization of passively sensitized skin sites

that although no one of the three commonest grasses (timothy, orchard and red top) invariably desensitizes to the two others, crossed reactions

out the clinical observation of the overwhelming consequence of ragweed in fall hay fever.

Among the mold spores producing respiratory

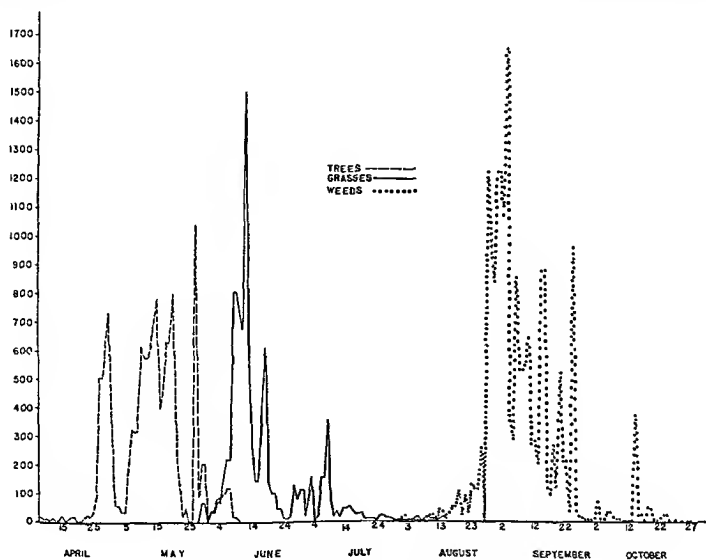


FIGURE 6. Average Pollen Counts at Newton Center.

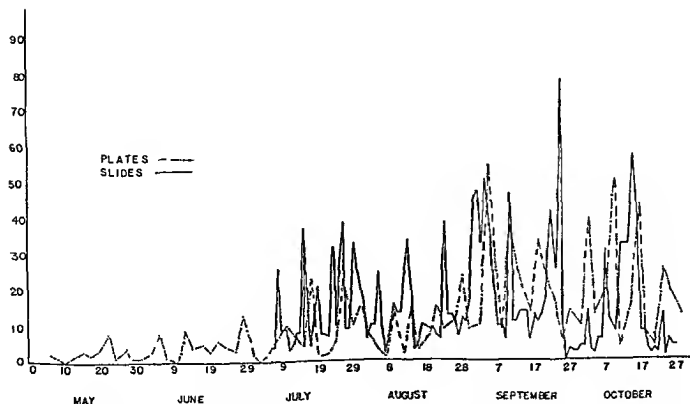


FIGURE 7. Average *Alternaria* Counts at Two Boston Stations, Newton and Worcester.

between the different species are very common.

The weed pollens consisted of ragweed (92 per cent), goldenrod (4 per cent), cocklebur (3.2 per cent) and wormwood (0.8 per cent). This bears

allergy, *Alternaria* is the commonest.<sup>6</sup> Figure 7 summarizes the results for the four stations at which exposures of slides and plates were made regularly (two Boston stations, Newton Center

and Worcester). To produce more consistent curves, the chart was constructed by adding the daily slide counts of the four stations and graphing the daily total as a solid line. The sum of the plate counts is represented as an interrupted line. Therefore, the curves are four times higher than they would be for a single station. Although the two curves do not superimpose, they are both of the same order of magnitude, the slide counts averaging slightly higher, and show the same seasonal fluctuation. The total counts for the season from the four stations gave essentially the same results except that the total for Newton Center was somewhat greater than that for the city.

The *Alternaria* season does not have such definite time limits as the pollen seasons. As shown previously,<sup>5, 6</sup> *Alternaria* can be cultured from the air in Boston throughout the entire year, but the heaviest contamination comes with the onset of warm weather, in July, when the grass counts are dwindling. The season reaches its peak with the weeds but persists into November long after ragweed pollen has left the air.

It will be noted that the counts of *Alternaria* here recorded are low compared with the pollen counts. However, the spores probably settle out of the air considerably more slowly than pollen because they are smaller and irregular in shape. Stokes's law does not apply to the calculation of their rate of fall, since they are not spherical. It seems probable that the per cubic yard contamination of the air with *Alternaria* spores is not much less than that of ragweed pollen in late August and early September.

## SUMMARY

A survey of the pollens producing hay fever in southeastern New England shows three clearly defined seasons: trees from April 19 to May 30, grasses from early June to mid-July, and weeds from August 20 to late September. The *Alternaria* spore season overlaps the grass and weed seasons and persists later into the autumn.

Grass and weed pollens are more abundant in suburban areas than in the city, whereas tree pollen is equally plentiful in town and city because of the numerous shade trees in the areas of the city studied.

Failure of pollen peaks from neighboring stations to be superimposed consistently demonstrates the effect of local vegetation and wind currents.

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## MEDICAL PROGRESS

### PHYSICAL THERAPY

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BOSTON

ONE of the outstanding events in physical medicine during the last two years was the publication of an excellent textbook by Krusen.<sup>1</sup> There has long been a need for a reference book to which the student or practicing physician could turn for sound and detailed information on the practical aspects of physical therapeutics. Krusen is an authority on the subject, and has had unusually large experience in clinical application and investigative work. In addition to comprehensive presentations of the subjects of heat, light and electrotherapy, he has included the technic and indications for the use of hydrotherapy, massage and exercise—measures that have received little acclaim recently because of enthusiasm concerning electrical apparatus, which actually have only a small role in physical therapy. The present knowledge of the physical and physiologic principles involved has been summarized, with extensive references. The illustrations and explanations of simple measures that may be used in the home are especially valuable.

Hypothermia has recently been found to have more new useful applications than any other physical measure. Many investigative studies have dealt with the physiologic changes and therapeutic effects of the reduction of general body temperature and the local use of cold. The present status of this therapy has been reviewed by Talbot.<sup>2</sup>

Recent developments in the use of the majority of other physical agents are presented in relation to the different medical specialties.

### MEDICINE

In the treatment of rheumatoid arthritis and degenerative joint disease, physical measures continue to have a significant role. In these conditions with a tendency to chronicity, simple procedures that can be carried out in the home should be emphasized. Krusen<sup>3</sup> has outlined specific instructions for the use of homemade brakers, clamp lamps, hot paraffin packs, whirlpool baths and contrast baths. Massage, when skillfully adminis-

tered on nonacute joints, is beneficial, and a lay person with proper instruction may learn simple techniques that are of value in improving local circulation and in relieving muscle spasm. It is recognized that training in body mechanics is effective in preventing undue strain and trauma on diseased joints.<sup>4</sup> Postural and specific graded exercises for increasing joint range and muscle power are probably of more benefit than any other physical measure when properly supervised.<sup>5</sup> Diathermy,<sup>6</sup> cabinet baths and more elaborate types of treatment have a place in hospital departments.<sup>7</sup> However, results of fever therapy in rheumatoid arthritis and osteoarthritis have been disappointing.<sup>8</sup> Iontophoresis with histamine and acetyl beta methylcholine chloride has given encouraging results,<sup>9-12</sup> but has not replaced other simpler agents for symptomatic relief. Neurologic symptoms may accompany cervical degenerative arthritis, and much benefit may be obtained by heat, massage, traction, manipulation and posture training.<sup>13</sup> The temporomandibular joint is frequently involved and often is not treated adequately. Bayles and Russell<sup>14</sup> brought out the necessity of complete rest and local heat during the acute stages, with mild gum-chewing exercises later. Coccygodynia, when caused by spasm of the levator ani, coccygeus and piriformis muscles, has frequently been relieved by internal massage, according to the experience of Krusen and Basom.<sup>15</sup> They also reported success from firm massage over the fibrous nodules, in addition to local heat and stretching exercises, in the treatment of fibrositis.

Short wave diathermy has been reported as curing lung abscess in 85 of 123 cases in the literature, as reviewed by Brugsch and Pratt.<sup>16</sup> In 8 cases, however, applications for ten to forty five minutes were given without effecting a cure. Only 2 of these cases were acute, and this method of treatment may deserve further trial in the acute stage. In spite of the steadily improving results of chemotherapy for pneumonia, diathermy is still thought to be a valuable adjunct in treatment, since it decreases cyanosis by improving pulmonary circulation.<sup>17</sup> Overdosage is to be avoided because of the possible edema.

In the management of cardiac conditions during convalescence, a carefully supervised, indi-

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vidual program of physical measures is beneficial.<sup>18</sup> This may consist, at first, in gentle stroking and passive motion of the extremities, followed later by graded active exercise to improve peripheral circulatory efficiency.

### GENERAL SURGERY

The aim of physical therapy in traumatic conditions is to shorten convalescence and rehabilitate the patient. In fractures, the early use of measures to soften or eliminate induration, diminish swelling, and lessen redness and heat ensures early function.<sup>19</sup> Elevation, gentle stroking, sedative massage, prolonged mild heat and assisted active exercise without pain may accomplish this.<sup>20-24</sup> The frequency of treatments is of some economic importance. Butler<sup>25</sup> has recommended daily treatments so long as there is progress, as measured by careful observations. Occupational therapy may then take over and speed return to work. Contusions of muscles may lead to myositis ossificans and prolonged disability. Preventive measures should be used in the early stages to control hemorrhage by cold applications and a compression bandage; massage on severe tender contusions should be avoided. Later, heat aids in the absorption of the hematoma.<sup>26</sup> Injuries involving tendons and nerves, particularly of the hand, should be splinted in a position of physiologic rest, care being taken to avoid tension on sutures.<sup>27</sup> Experimental studies of the tensile strength of healing tendons have revealed that motion should not be started until after sixteen days; it should then be restricted for two weeks more, when free active motion is safe.<sup>28</sup>

In the treatment of peripheral vascular disease, the value of alternate positive and negative pressures, by means of a leg boot and intermittent venous occlusion, appears to be limited.<sup>29</sup> The careless use of local heat, particularly diathermy, is dangerous, since the metabolic requirements may be increased beyond the circulatory capacity and gangrene may develop.<sup>30</sup> When heat is indicated, either a thermoregulated cradle or reflex heating by warming the upper extremities or by applying diathermy over the sacral areas is desirable.<sup>31, 32</sup> Iontophoresis with acetyl-beta-methylcholine chloride does not replace surgical measures for varicose and post-thrombophlebitic ulcers, but after simpler methods have failed, some discomfort may be relieved by this means and healing promoted.<sup>33, 34</sup> Buerger's exercises continue to be a valuable adjunct in treatment when carefully prescribed,<sup>35</sup> and the oscillating bed tends to effect the same results when active exercises are impossible.<sup>36</sup>

Since the advent of extensive chemotherapy,

local measures have assumed less significance in the treatment of genitourinary infections. Diathermy, however, is still useful for symptomatic improvement in chronic prostatitis and pelvic inflammatory disease.<sup>37</sup>

A major part of treatment following thoracoplasty is the prevention of scoliosis and limited painful motion of the shoulder girdle and arm. A carefully graded set of exercises with skillful supervision gives gratifying results.<sup>38</sup>

The sterilization of air in the operating room by means of ultraviolet radiation has been studied, and methods have been developed whereby it is claimed that contamination from unsterile air can be practically eliminated.<sup>39-42</sup> Similar methods have been valuable in reducing the incidence of respiratory-tract infections on hospital wards.<sup>43-45</sup>

### ORTHOPEDIC SURGERY

The problem of chronic backache and sciatic pain has not been solved, as indicated by the numerous publications recommending different treatments. A recent symposium<sup>46</sup> on diagnosis and treatment has been published and contains much valuable information concerning the relation to backache of posture, visceral disease, fractures and other trauma, faulty mechanics and inflammatory processes. Surgical and conservative measures in treatment are discussed. Kuhns<sup>47</sup> reports the relief of sciatic pain and low-back disability in 771 of 1000 cases by means of rest on a flat bed with hips flexed for ten days and daily application of heat, followed by graded exercises and support when the patient is ambulatory. The different physical measures indicated in backache from various causes include traction, manipulation, special stretching and postural exercises, massage, particularly firm massage in fibrositis, and local application of heat.<sup>48</sup> Corsets are frequently helpful, and the proper types to be used have been discussed by Ober.<sup>49</sup>

A specific exercise program is of distinct value in the treatment of scoliosis. Colonna and vom Saal<sup>50</sup> found that 30 per cent of 500 cases of poliomyelitis developed scoliosis. The presence of asymmetrical paralysis and inadequate support were important factors in its development. Muscle-training and chest-expansion exercises were helpful, but spinal fusion was usually indicated in the presence of moderate and severe deformity. Conservative treatment in carefully selected cases has been successful in Steindler's<sup>51</sup> experience. The lumbar and cervicothoracic sections of the spine were limbered up to promote derotation and the development of countercurves to establish compensation. Adequate musculature was essential for success. In those cases requiring fusion, the



physical therapists are called on for special limbering and manipulative treatments prior to operation.<sup>52, 53</sup>

In deformity of the back due to juvenile kyphosis, physical measures are relied on almost exclusively in treatment. These consist in support, rest, local heat, light relaxing massage and corrective exercises of graded intensity.<sup>54</sup> Wheeldon<sup>55</sup> has suggested that contracted hamstring muscles may have a role in the production of poor posture and juvenile kyphosis. Fifty per cent of his cases were improved by passive hamstring stretching and remained improved. Twenty-five per cent tended to recur when the exercises were stopped. The remainder were unaffected by exercises. In this last group, he has had success by resection of the hamstring muscles.

Orthopedists and physical therapists have frequently expressed the advantages of good posture. Joplin<sup>56</sup> has applied the principles of posture in occupational therapy, which is a timely and worthwhile contribution. Most of the concepts of postural instruction are based on empirical evidence. A metabolic study, however, showed that the energy expenditure of standing was very small, and the sense of fatigue associated with motionless vertical posture may be due to cerebral anemia, which can be overcome by sway and relaxed stance.<sup>57</sup>

The chief development in the treatment of infantile paralysis that commands interest at present is the so-called "Kenny method." Briefly, this consists in nearly continuous daily hot fomentations during the acute stages to relax spasm, no splinting, early passive and active exercises without pain, and special muscle re-education, concentrating on the insertion of muscles, with attention to body mechanics. Kenny's theory is that the important features of acute poliomyelitis are muscle spasm, inco-ordination due to pain and substitution of muscle function, and mental alienation, because of which the patient forgets normal muscle performance or loses the idea of making muscles contract. Complete evaluation of this treatment is not possible, according to preliminary reports.<sup>58</sup> Certainly, quick recoveries have been observed, but it is too early to determine end results. Levin<sup>59</sup> has written a splendid book covering the many aspects of diagnosis and treatment of this disease.

The treatment of painful shoulders caused by bursitis is still unsatisfactory in spite of reports of success with novocain injections, saline irrigations, operative removal of calcium deposits, manipulation, rest, local heat, exercise and large doses of ammonium chloride.<sup>60-67</sup> A carefully

controlled study of these various methods is needed for proper evaluation.

Foot disabilities are common and are frequently due to mechanical strain. Training in proper use of the feet, special foot exercises, posture correction, contrast baths and proper shoes are measures recommended in prevention and treatment.<sup>68, 69</sup>

#### NEUROLOGY AND PSYCHIATRY

The most interesting recent development in the treatment of mental disease by physical agents is the use of electric-shock therapy. The first clinical work was done in the Rome clinic by Bini<sup>70</sup> in 1938 and by others.<sup>71</sup> The advantages claimed for this method over other types of shock therapy are simplicity, as compared with intravenous medication in overactive patients, immediate loss of consciousness, with amnesia for the whole treatment, and a low incidence of complications, with few fractures and systemic reactions. The apparatus used in this country by Myerson has been described by Feldman and Davis.<sup>72</sup> The current source is a 60-cycle alternating current with a controlled range of voltage from 50 to 130 and a milliamperage from 50 to 750. Metal electrodes, with electrode paste, are attached to both temporal regions with a head band. The average patient required 70 volts at 350 to 500 milliamperes for 0.1 second to produce a convulsion.

Meggendorfer<sup>73</sup> treated 40 patients with schizophrenia, with very good results in 10 and temporary improvement in 10 more; the others were not benefited. All eight patients with manic-depressive psychosis were improved. Gonda<sup>74</sup> reported 58 per cent remissions in 29 patients with schizophrenia, and 87 per cent recovery in 8 patients with manic-depressive psychosis. Myerson<sup>75</sup> states that the psychoses of choice for treatment are the marked continuous depressions, and that the treatments may be given in the home or office. In schizophrenia, this method has the same general value as the use of Metrazol, and the indications for treatment are the same. No neurologic sequelae have been observed, but Gonda reported the fracture of both humeri in 1 case. Precautions must be taken against fractures, as with any convulsive therapy, and the equipment must be tested before each treatment. The changes in the human central nervous system are unknown, since there have been no deaths. Bini,<sup>70</sup> however, has reported changes in animals that were in some cases irreversible, although not described in detail. Other observers have stated that the changes in animals were not so severe as those found after insulin hypoglycemia.<sup>71</sup>

Infantile cerebral palsy occurs in about 7 hirths

per 100,000 population a year and presents a problem in treatment. Spastic, athetoid and ataxic cases should be differentiated, since the treatment varies accordingly. Institutions where muscle re-education and schooling can be carried out together are most effective. Home therapy is very satisfactory in some cases but must be individualized, and the nature of the disorder and the personality must be understood by the family. The program of treatment consists essentially in special relaxation and co-ordination exercises, which must be persisted in daily and combined with occupation to form new habit patterns. Several recent publications<sup>76-82</sup> have been found helpful by parents and workers in the field.

The exact value of electrical stimulation in peripheral-nerve lesions to lessen atrophy and promote return of function is still problematical. In experiments on sciatic section in monkeys<sup>83</sup> and dogs,<sup>84</sup> it has been found that the degree of regeneration of peripheral nerve fibers and the atrophy and degeneration of denervated muscles are uninfluenced by physical therapeutic methods, including electrical stimulation. Massage and passive movement seemed most beneficial in securing maximum return of function, provided there was adequate splinting. Fischer,<sup>85</sup> however, showed in rat experiments that twelve to twenty minutes of intensive electrical stimulation produced a training effect in denervated muscles that lessened the degree of atrophy. Clinical experience has led most observers to consider electrical treatments beneficial in facial-nerve paralysis, but large series of cases and controls will be necessary to obtain more objective evidence of the value of electrical stimulation.<sup>86</sup>

#### DERMATOLOGY

The dermatologist is particularly interested in ultraviolet irradiation, because so many skin diseases have been given this therapy with both beneficial and deleterious results.<sup>87</sup> Blum<sup>88</sup> has recently made an outstanding contribution to the literature on the subject of light in relation to medicine. He carefully defined photodynamic action and described methods of investigation that should lead to more accurate studies in the future. Diseases due to light are considered in a separate section. It is essential that clinicians be aware of these conditions, since ultraviolet irradiation may be extremely dangerous, as in lupus erythematosus. Of late, the photosensitizing action of the sulfonamides has been frequently reported.<sup>89-91</sup> Sulfanilamide in high concentration sensitizes human skin to irradiation below 3200 Angstrom units, producing severe sunburn. This is not photodynamic action, and porphyrins are

not involved, but it probably represents an increased sunburn reaction. Patients receiving sulfonamides should therefore not be exposed to sunshine or ultraviolet lamps. This photosensitizing action of sulfanilamide has been used in the treatment of psoriasis to enhance the effect of ultraviolet irradiation, but is not recommended routinely because of the potential dangers.<sup>92</sup>

Several reports have appeared on the successful treatment of fungous infection of the hands and feet by copper iontophoresis. Hoechstetter<sup>93</sup> treated 18 cases, with healing in 16, giving five to nine treatments weekly, or twice a week when the infection was severe. Equally good results were obtained by Haggard, Strauss and Greenberg.<sup>94</sup>

#### OTOLARYNGOLOGY

Local heat in various forms gives some symptomatic relief from upper respiratory-tract infections. A simple infrared lamp is quite effective for this purpose. Short-wave diathermy has been used extensively for sinusitis, but does not effect a cure.<sup>95</sup> Better results are obtained in acute cases than in chronic ones, but postoperative results are disappointing. In the treatment of gingivitis, parodontosis and postextraction pain, short-wave diathermy gave relief in all 64 of Kobak's<sup>96</sup> patients. Ion transfer (iontophoresis), using zinc salts for hay fever, vasomotor rhinitis and chronic otorrhea, has not brought the cures first hoped for. Evidence for proper selection of cases awaits further investigation.<sup>97</sup>

#### FEVER THERAPY

Artificial fever continues to have a role in the treatment of syphilis, gonorrhea and chorea. The methods of production and effects have recently been summarized.<sup>98</sup> Results and hazards are about equal with inductive heating, hot moist air and hot sprays of water.

In general paresis, results have been slightly better with artificial fever than with malaria.<sup>99</sup> Solomon, Kopp and Rose<sup>100</sup> have tried the effect of increasing the temperature swing during a six-hour period by first reducing the temperature to 90°F. under Pentothal anesthesia with ice packs, and then inducing a fever of 104 to 105°F. They have as yet made no conclusions of its value.

The sulfonamides have subordinated fever therapy in the treatment of gonorrhea, but the percentage of resistant cases has been reported from 10 to 20.<sup>101-103</sup> These results are about the same as those of fever alone. The combined use of sulfanilamide and fever, however, has given nearly 100 per cent cures.<sup>104-107</sup> Medication for eighteen to forty-eight hours prior to fever therapy has been recommended. A single ten-hour fever at

106 to 107°F has then been sufficient to obtain negative cultures

Good results of treatment of eborca by artificial fever continue to appear<sup>108-110</sup> Short sessions (two and a half to three hours) at 104 to 105°F are repeated daily or on alternate days for a total of about twenty to thirty hours of fever as the usual routine Bennett and Hochstra<sup>110</sup> had excellent responses in all 17 of their cases, Elkins and Krusen<sup>109</sup> reported only a single failure in 20 cases adequately treated

Hyde<sup>111</sup> has tried short (one hour or less) and mild (up to 103°F) fevers in allergic diseases with interesting results Thirty two patients were treated, with improvement in 75 per cent of the asthma cases and 81 per cent of the hay fever cases

An increase in temperature from 98 to 103°F has been shown to increase the bacteriostatic power of sulfanilamide about one hundred times<sup>112</sup> With this in mind, combined fever and chemotherapy has been tried in subacute bacterial endocarditis Bierman and Bachr<sup>113</sup> treated 16 cases with 2 cures, two years and ten months, respectively, after treatment Krusen and Bennett<sup>114</sup> reported 6 unsuccessfully treated patients A review of the literature<sup>115</sup> revealed that among 200 cases due to *Streptococcus viridans* and nonhemolytic streptococcus, 6 per cent of the patients recovered after administration of sulfonamides Of 43 patients treated with heparin and chemotherapy, there was 12 per cent recovery Among 24 patients treated by chemotherapy and artificial fever, 4 recovered Of 21 patients treated by chemotherapy and typhoid paratyphoid vaccine, 5 recovered, an incidence of 25 per cent These results are encouraging, but not conclusive, because of the small number of cases and short follow up periods in some

#### PHYSIOLOGY AND BIOPHYSICS

Numerous reports have appeared of research on the physiologic effects of heat, light, electricity and other physical agents Bisgard and Nye<sup>116</sup> found that gastrointestinal motor activity, as indicated by kymographic recordings, was inhibited by the application of heat to the abdominal wall and by ice water taken by mouth Stimulation resulted from application of ice externally and from ingestion of hot water by mouth Another study on the effects of hot and cold applications revealed that the nasopharyngeal irrigations at temperatures above 41°F and below 113°F caused no marked variation in cervical lymph flow At temperatures of 41°F or below and at 113°F or above, the lymph flow increased during the ap

plication or for longer periods if the capillaries were damaged<sup>117</sup> Gammon and Starr<sup>118</sup> investigated the relief of pain by counterirritants and found that the intermittent application of heat and cold was much more beneficial than the use of either agent alone Changes in circulation did not explain the relief of pain, in animal experiments, action potentials from sensory nerves were altered, suggesting a neural mechanism

The cardiovascular effects of heat have been reviewed by Bazett,<sup>119</sup> and the present knowledge of the effect of heat, massage and exercise on lymphatic circulation has been authoritatively discussed by Drinker<sup>121</sup> Diathermy has been shown to have no thermic effects on blood pressure<sup>122</sup> or intestinal activity<sup>123</sup> in animal experiments It was useful in raising the cutaneous temperature of feet reflexly by application to the trunk<sup>124</sup>

In studying reactive hyperemia, Abramson and Ferris<sup>125</sup> found that local heat to the hand was a more potent stimulus than tissue anoxia from ten minute circulatory occlusion, whereas the reverse was true in the forearm and leg Five minute circulatory arrest resulted in relatively complete vasodilatation, according to Eichna and Wilkins,<sup>126</sup> and the reactive hyperemia was only slightly increased by local heat at 104°F or prolonged ischemia (ten to fifteen minutes)

Iontophoresis may cause small but slowly healing burns in spite of the usual precautions Moltor and Fernandez<sup>127</sup> made a careful experimental study of the problem and recommended definite current values for electrodes of various sizes They have expressed this relation of safe current to electrode size in the form of a graph, which should be of value in improving technique and in preventing burns

Other studies on technique and dosage have been reported in relation to short wave diathermy These should be of interest to technicians and have been abstracted in detail by Kovács.<sup>128</sup>

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 27401

#### PRESENTATION OF CASE

A forty-seven-year-old Greek laborer was admitted to the hospital because of a recurrent pain in the chest, accompanied by shortness of breath and general poor health of nine days' duration.

He had been followed in the Out Patient Department for ten years because of recurring attacks of pain, which radiated over the entire anterior part of the chest, the scapular area and both arms. Since the blood Hinton and Wassermann reactions were strongly positive, antisiphilic therapy was given on several occasions. In all, about two hundred injections of either arsenic or bismuth (mainly the latter) had been given, followed by Mapharsen in small doses. Eight months before admission, the blood Hinton reaction remained positive, although the Wassermann reaction was negative. From the time that the patient was first studied, his heart and great vessels had been enlarged, and he had had an auricular flutter with variable block, usually approaching 4:1. A to-and-fro murmur was always present, loudest in the third left intercostal space. The blood pressure ranged around 140 systolic, 70 diastolic, until the last year, when the diastolic pressure failed, with resultant increase in pulse pressure.

At first, x-ray examination showed dilatation and increased pulsation of the aorta, accompanied by considerable dilatation and pulsation of the pulmonary conus and the hilar shadows. Subsequent roentgenograms demonstrated interesting changes in that the shadow of the heart margin became markedly irregular just above the apex, while the pulmonary conus and ascending aorta appeared to be involved in a double mass. The pulsations of this mass were less vigorous than those of the apex of the heart. The trachea was displaced to the right, and the left main bronchus was unusually small and irregular. On still another roentgenologic examination it was thought that definite, multiple, pulsating saccular dilations extended both anteriorly and posteriorly from the root of the aorta. There was an apparent slight erosion of the left fourth rib near the costochondral junction.

Until entry into the hospital, the patient had remained free from pulmonary congestion, club-

bing of the fingers, ankle edema and cough. He continued at heavy labor with pick and shovel until the last two weeks before entry, although he was cautioned repeatedly against doing so. Two years before the time of his final episode of illness, he had been digitalized, and had continued on this drug intermittently.

Nine days before hospitalization, there was a vague onset of ill health. A day or so later, the old chest pain returned. The patient had been free of this for a long time previously. Simultaneously, he began to experience shortness of breath, and difficulty in getting his breath. On the fourth day before entry, he began to redigitalize himself (having been without digitalis for at least two weeks). The following day he took to his bed. Because of exacerbation of the chest pain, his physician prescribed morphine and nitroglycerin, but neither drug afforded relief.

The past history was significant in that the patient had been a marathon runner while in his twenties. There was a definite history of a penile sore. His family history was irrelevant.

On physical examination, the patient was found sitting upright in bed in some respiratory distress but free from cyanosis. The heart was markedly enlarged, with an increase in the supracardiac dullness. A slight systolic thrill was felt over the third left interspace with a corresponding loud systolic murmur and softer diastolic murmur best heard in this area. There were marked pulsations in the veins of the neck. A loud friction rub was present over the left anterior chest above the heart, together with many coarse, crackling rales, which extended along the sternal border. Some dullness, without rales, was manifested at each pulmonary base. The blood pressure was 140 systolic, 40 diastolic. The pulse was of Corrigan type, with a rate of 84. The rhythm was totally regular at times, and irregular at others. The liver and spleen were not enlarged, and there was no peripheral edema.

The rectal temperature was 102°F., and the respirations 36.

Examination of the blood showed a white-cell count of 13,900 with 90 per cent polymorphonuclears, and a red-cell count of 5,150,000 with 90 per cent hemoglobin. The blood Wassermann and Hinton reactions were positive.

An electrocardiogram showed depression of the ST takeoffs in Leads 1 and 4, and their elevation in Lead 3. The ST segment sagged in all leads, and T was deeply inverted in the first three leads. No axis deviation was present.

An x-ray film showed the heart shadow to have enlarged about 2 cm. since examination in the clinic a month previously. The shadow in the

area of the great vessels was also larger. The left lower lobe of the lung appeared collapsed, with increased aeration of the left upper lobe.

During the night, the patient rested fairly well, although the pain in his chest was only partly relieved by sedatives. The respiratory rate slowed.

The following afternoon, he was found in coma, from which he could not be roused. He was cyanotic, breathing deeply and irregularly about four times per minute. The heart sounds were faint, at 20 per minute. Neither pulse nor blood pressure could be obtained. The patient was given adrenalin and coramine, and rallied slightly. He became restless, and complained of pain in his abdomen. Administration of oxygen improved his color, but both heart and lungs failed within fifteen minutes.

#### DIFFERENTIAL DIAGNOSIS

DR. HOWARD B. SPRAGUE: It seems as if the fundamental situation here must be related to a syphilitic infection. The patient had received a good deal of antisymphilitic therapy. On the other hand, his cardiovascular examination was apparently abnormal by the time he started this treatment. The diagnosis of the anatomic changes appears to rest largely on the x-ray examination. It is true that all this time there was a to-and-fro murmur, loudest in the third intercostal space, which may have been due to true syphilitic involvement of the aortic valve, with aortic regurgitation. One must accept this description, although the murmurs were somewhat more obvious to the left of the sternum. It is fair to say that this does represent aortic regurgitation because we have the statement that he had a Corrigan pulse, although his diastolic pressure was maintained at 70 until the last year before entry, when it finally dropped and the pulse pressure increased. It sounds, then, as if there had not been a high degree of aortic regurgitation. The main pathologic lesion lay beyond the aortic valve.

I should like to have Dr. Schatzki tell me about this x-ray examination, because at one time we are told that the shadow of the heart's margin became markedly irregular, and later on it was thought that definite, multiple, pulsating sacular dilatations were present. I wonder if these sacular dilatations of the aorta made the margin of the heart shadow irregular.

DR. RICHARD SCHATZKI: When one reads the story and hears about the aortic signs and about syphilis, everything seems to be simple. Aortic aneurysm is the first diagnosis. The films, however, are disturbing because they look different from those seen in the usual aortic aneurysms. The lesion is fairly well described in these re-

ports. The striking thing is that this mass lies anteriorly, which means, if it is connected with the aorta, that it comes from the ascending aorta. Usually, if there is an aneurysm of the ascending aorta, it is on the right side of the heart in the anteroposterior films. The abnormality in the anteroposterior film in this case is almost exclusively on the left side. What lies in this area on the left side anteriorly? If it has anything to do with the vascular system, there are two possibilities. One is the pulmonary artery, and the other is the aorta, which is quite close to the pulmonary artery. Which of the two is it? Films taken later show that this mass had grown, but it remained in the same position anteriorly.

DR. PAUL D. WHITE: What is the interval between those two films?

DR. SCHATZKI: Two years. This is a film that was taken on the last day. It is important because it shows the mass and, within the shadow of the mass, a structure that has the appearance of the left hilus or pulmonary artery before it enters the hilus. It would be unusual for the pulmonary artery to be visible if the mass arose from the pulmonary artery.

DR. SPRAGUE: You do not say that this is the pulmonary artery.

DR. SCHATZKI: Not necessarily; but I think it is. I can speak freely because I do not know this case. I am in the same predicament as you. I think what we see within the shadow of the mass is the pulmonary artery or pulmonary conus. The fact that it projects out so far does not necessarily mean that it was enlarged. It may have been pushed over. These films were apparently taken after the last episode. They are not comparable with the first films, because they are taken in a horizontal position. The heart shadow has markedly increased in size, and the mass has still further increased in size even considering the magnification; the aortic shadow seems a little larger. This man had an enlarged heart in the region of the left ventricle and a mass apparently connected with the large vessels, which, so far as its position is concerned, could have arisen from the pulmonary artery, but from these films alone I think it is more likely that it arose from the left border of the ascending aorta.

DR. SPRAGUE: Dr. Schatzki and I agree, anyway. I am not going to be led off the trail by the fascination of syphilitic involvement of the pulmonary artery. We know that when we have thought that sort of thing was present we have been fooled. We are, I think, on safer ground if we say that this was an unusual aneurysm, which arose just above the aortic valve, with a certain amount of dilatation of the root of the

aorta and with some aortic regurgitation, and that the systolic murmur was probably produced in this aneurysmal sac. It undoubtedly displaced the pulmonary artery, and it produced a constriction of a bronchus, resulting in collapse of the left lower lung, but I do not see enough in the picture pointing to trouble in the pulmonary circuit to make me consider this an aneurysm of the pulmonary artery, or perforation from the aorta into the pulmonary artery. There was a growth of this aneurysmal sac, with pain from actual erosion of the chest wall.

Let us discuss a few points in detail. It is unusual for a patient with a syphilitic heart to have auricular flutter. Of the patients autopsied here who have been studied electrocardiographically, I can recall only one with auricular fibrillation. One notes that there were marked pulsations in the veins of the neck, which I assume must have been caused by tricuspid regurgitation. There is no note that these resembled rapid flutter waves. The electrocardiogram shows inversion of the T waves in all three leads, with a depression of the ST takeoffs in Leads 1 and 4 and an elevation in Lead 3, all of which are suggestive, I should think, of some left ventricular strain, even though there is no increase in QRS with a downward direction in Lead 3, which is characteristic of left-axis deviation. That is not too unusual in syphilitic aortitis. About half the patients who have syphilitic aortitis with aortic regurgitation have normal electrical axes, as judged from the direction of QRS. There have been occasional cases of bundle-branch block, both right and left, and an occasional case of right-axis deviation, but in that event there has always been a complication. In this particular case, there might be, I suppose, the added strain on the right side of the heart, if there were an aortic aneurysmal sac distorting or compressing the pulmonary artery, which might lead to some balancing effect in the electrocardiogram.

The final episode is probably explained by the story of what appears to be an enlarging aneurysmal sac, with pain, friction rub and some leukocytosis. It is fair to say that the cause of death was a rupture of the aneurysm. If the aneurysm ruptured into any place where free bleeding could result, whether into a pleural cavity or into the esophagus, trachea or bronchus, I think that the patient would have died sooner than he did. A final x-ray report mentions a marked increase in the heart shadow, and there is a note that the heart sounds were faint, with marked bradycardia. Neither pulse nor blood pressure could be obtained. There is the syndrome of cardiac tam-

ponade. The position of the aneurysm suggests that it ruptured into the pericardium. I am going to assume that that is what happened. In view of the position of this sac at the very base of the aorta, one could guess that there would be some obstruction in the region of one or the other coronary ostia. It does not quite seem as if he had an acute coronary closure as the final episode, although I imagine that that might be possible, or that perforation might in some way have resulted in further compression of the coronary artery. I therefore believe that this was a syphilitic aortitis, with aneurysm of the first portion, presenting to the left and anteriorly, and with final rupture into the pericardium.

DR. WHITE: Just to corroborate Dr. Sprague's opinion about the rarity of pulmonary-artery syphilis and pulmonary aneurysm, I want to say that the most important case that we followed for some years, believing that this was the diagnosis, proved at autopsy to have an aortic aneurysm presenting in the region of the pulmonary artery. That is also true of several other cases on record. Thus, our experience with pulmonary-artery aneurysm has thus far always been disappointing. There is, I think, some suggestion, as Dr. Sprague mentioned, that the pulmonary artery or its branches were compressed by an aortic aneurysm, thereby increasing the size of the main trunk and major branches of the pulmonary artery, along with a shift in position to the left. An increased pulmonary-artery pressure might have overburdened the right ventricle, accounting for the increased pulsation of the neck veins. Another explanation of increased fullness of the neck veins would be mediastinal compression by the aneurysm; that is not so likely, however, because there would then have been engorgement, with little or no venous pulsation. Rupture of the aorta into the pulmonary artery would have produced a continuous murmur, which was not present in this case, and rupture into the superior vena cava would have caused a marked increase in pulsations in the neck veins and also a continuous murmur, which was not present. One case of rupture of the aorta into the pulmonary artery, which was correctly diagnosed before death, had a continuous murmur that made the diagnosis possible. Also, rupture of the aorta into the superior vena cava would have been attended by overwhelming symptoms and a much shorter life than this patient had after the episode. I agree that death in this case was probably due to cardiac tamponade. Hemorrhage into the pericardium is often rather slow and allows a good many hours before death occurs.



## CLINICAL DIAGNOSES

Pulmonary embolism.  
 Syphilis  
 Syphilitic aortitis.  
 Aortic aneurysm?  
 Aneurysm of pulmonary artery?  
 Dissecting aneurysm?

## DR. SPRAGUE'S DIAGNOSES

Syphilitic aortitis, with aortic regurgitation  
 Aneurysm of ascending aorta, with final rupture  
 into the pericardium.

## ANATOMICAL DIAGNOSES

Syphilitic aneurysm of the aorta, with rupture  
 into the pericardium and pulmonary artery  
 Hemopericardium.  
 Syphilitic aortitis.  
 Pulmonary atelectasis  
 Hydrothorax, left.

## PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: This man did have a syphilitic aneurysm of the ascending aorta, which presented anteriorly, as suggested by Dr Sprague and Dr Schatzki. At the time of autopsy it measured 10 by 7 by 4 cm, quite a sizable aneurysm, filled, as usual, with a laminated thrombus. It covered most of the left auricle and presented more anteriorly than any we had seen before. It had ruptured from its posterior aspect into the pericardial sac just below the reflection of the pericardium, and there was 1000 cc of fresh blood in the cavity. The aneurysm was apparently adherent to the pulmonary artery before rupture, because it also ruptured terminally into the pulmonary artery. The left lower lobe and lower portion of the upper lobe were collapsed, apparently because of pressure on the bronchus by the aneurysm, and there was 1000 cc. of straw-colored fluid in the left pleural cavity. The syphilitic aortitis apparently had not extended down to the aortic valve itself, since there was no separation of the cusps at their commissures, and nothing that would indicate that the patient had aortic regurgitation. The coronary mouths were not constricted. The mouth of the aneurysm was located 1.5 cm above the valve, and the tear into the pulmonary artery had occurred 35 cm above the pulmonary valve. The heart was not much enlarged.

DR. SPRAGUE: Was there no obvious increase in the size of the right ventricle?

DR. CASTLEMAN: No; the right wall measured 3 mm.

DR. WHITE: That leaves open the explanation of the diastolic murmur. I suppose it is possible that during life the aortic ring was dilated, allowing some regurgitation that was not apparent when the aorta collapsed after death. The aneurysm was very low in position, was it not?

DR. CASTLEMAN: Yes.

DR. WHITE: It has been my conviction for some time, but this is not generally recognized so far as I know, that in a good many patients with syphilitic aortitis the aortic regurgitation is due, not to a structural change in the valve, but to a dilatation of the very first part of the aorta, involving also the aortic ring. This is much more evident during life than at autopsy.

DR. SPRAGUE: That is borne out by the autopsies here. I have been going over them. There has frequently been no involvement of the valve, even though the medical records continuously report signs of aortic regurgitation.

## CASE 27402

## PRESENTATION OF CASE

A sixteen-year old American schoolgirl entered the hospital complaining of a skin eruption.

Four months before entry, the patient noted on each cheek a patch of redness that was associated with burning. The lesions spread until they crossed the bridge of the nose and assumed a butterflylike outline. Three months later, the redness had spread to her forehead. Two weeks before entry, while taking a bath, she noticed that there were red spots on her feet, and on further examination some were found on her back. Four days before admission, she developed a temperature of 101°F, and a few days later noted red patches in her mouth. Her weight had dropped from 150 to 132 pounds. Otherwise, she had been quite well, except for some loss of energy.

The father, mother and two siblings were living and well. There was no history of tuberculosis.

The patient had eczema as a baby and the other usual childhood diseases, including measles, pertussis, scarlet fever, diphtheria, chicken pox and mumps. She had spontaneous nosebleeds about once a month. There was no history of chest pain, night sweats or cough.

Physical examination showed a well nourished, cheerful girl not acutely ill. The face revealed a masklike involvement, which excepted the mouth, eyes and hair margin. The lesion was described as a dusky erythema of a peculiar purplish hue, yellowish red at the outer margins. It was dry throughout, with a tendency to a fine, grayish scaling. The ears were involved, but the scalp

was free. There were hemorrhagic crusts in the nose. The buccal mucous membrane was denuded in several areas, and the hard palate ulcerated. The lesions were all rather sharply limited. The face was slightly tender and warm. There were a few reddened areas on the back and over the sternum. The tips of the fingers were reddened and slightly swollen. The cervical and left inguinal lymph nodes were enlarged and moderately tender. The edge of the spleen was felt on deep inspiration.

The temperature was 99°F., the pulse 90, and the respirations 20.

Examination of the urine was negative. The blood showed a red-cell count of 4,180,000 with a hemoglobin of 85 per cent and a white-cell count of 5800 with 56 per cent polymorphonuclears. The blood Hinton reaction was negative. The bleeding time was 2 minutes, the clotting time 2 minutes.

During the first week, the patient improved. The white-cell count, which had fallen as low as 2600, rose to 4000. The edema of her face was less marked, and the erythema of the lesions had subsided. About one month after admission, she had a slight fall in her white-cell count that was consistent with new lesions and swelling of the face. She was given nucleotide therapy for about two weeks, without any improvement. She developed generalized choreiform movements, particularly involving the left side, which persisted until death. She had weakness of the left hand, with circular movements. The knee jerks were active. She received x-ray treatment for her skin lesions, with remarkable improvement. After the development of choreiform movements, it was learned that the patient had been treated by a physician one year before entry for nervousness because "she could not sit still a minute." She developed a soft systolic murmur, which was believed to be hemic in character, probably owing to her secondary anemia. The temperature ranged from 99 to 102°F., and shortly after the third month of her stay it rose to 104°F. and she complained of headache, without any local signs or symptoms. Then the temperature rose to 105°F., and she became quite prostrated and dull and complained of a "funny feeling" in her head. The skin was hot and moist, and the skin lesions became redder. She developed pain in the right ear, and examination showed slight edema along one edge of the drum. A pericardial friction rub was heard for the first time. She rapidly failed, became semistuporous, and died three and a half months after admission — seven and a half months after the onset of her illness.

#### DIFFERENTIAL DIAGNOSIS

DR. WALLACE ZELLER: The presence of acute disseminated lupus erythematosus is occasionally unsuspected because of the absence of the skin lesions so frequently found in this disease. In the case under discussion, no such oversight could occur. The skin lesions as described were quite consistent with this diagnosis, and numerous other features presented by this patient were also compatible. The patient belonged to the age group and sex most commonly affected by this disease, and the fever, weight loss, mucous-membrane lesions, lymph-node enlargement, redness and swelling of the fingertips, edema of the face and enlargement of the spleen are all characteristic findings in this widespread constitutional malady. We do not know definitely how long this patient had been troubled with spontaneous nosebleeds, so that their significance cannot be accurately weighed. Since purpura or other hemorrhages were not noted during the course before death, one is not justified in assuming that the nosebleeds were due to thrombocytopenic purpura, which is sometimes associated with systemic lupus erythematosus. The leukopenia, which was consistently found, is, of course, quite characteristic. The soft systolic murmur was thought to be of hemic origin. The degree of anemia at the time this murmur appeared is not stated. Such murmurs, however, may be caused by the endocarditis that sometimes accompanies acute disseminated lupus erythematosus. Their presence in other patients has, in fact, often led to an erroneous diagnosis of rheumatic fever. The terminal occurrence of pericarditis in this patient is the only evidence of involvement of the serous membranes. Headache such as she complained of has been noted in systemic lupus erythematosus, usually without any other evidence of involvement of the nervous system. It is possible that otitis media developed a short time before death. It might have been associated with a hemolytic streptococcus infection, which is often a terminal event in these patients.

There is much in this case history, therefore, to support a diagnosis of acute disseminated lupus erythematosus. Three items deserve special comment, however, since I believe they are unusual in this disease: First, the urine was described as normal, and it is implied that the patient had at no time demonstrated urinary abnormalities. Clinical evidence of renal disease is almost a constant feature of acute disseminated lupus erythematosus. Although it has occasionally been shown that kidney involvement may occur without clinical manifestations in this disease, evidence of its absence here must be weighed seriously in con-

sidering the diagnosis. Secondly, the presence of choreiform movements is, so far as I know, unusual in acute disseminated lupus erythematosus. Convulsions do appear in some cases shortly before death, but I know of none in which chorea has been described. The type and degree of involvement of the nervous system in disseminated lupus is not well known anatomically. Since the disease does involve the nervous system, however, and since widespread damage to small vessels is commonly found, it is not improbable that choreiform movements might occur. They would admittedly be very unusual. Thirdly, it is stated that improvement in the skin lesions followed x-ray therapy. Exacerbations of systemic lupus erythematosus following exposure to ultraviolet rays are well known. Similar exacerbations following roentgen-ray treatment have also been observed. It would be very unusual for exposure to x-rays to be followed by remission rather than exacerbation of the rash. It is not improbable that roentgen therapy was given to this patient on the chance that she might have mycosis fungoides. The fact that her skin improved temporarily following treatment is in favor of such a diagnosis rather than systemic lupus erythematosus. It should be noted, however, that x-ray treatment was not continued and was not tried again when the patient had the terminal exacerbation with further skin involvement. Apparently, the former benefits of the x-ray treatment were not considered to be very striking, or some contraindication to its use was thought to be present.

It is evident, then, that these three unusual features are of only relative importance in diverting us from a diagnosis of systemic lupus erythematosus. The disease can occur without clinical evidence of renal involvement.

Are there other diseases that should be considered in the differential diagnosis? Certainly, Sydenham's chorea in association with rheumatic fever and carditis should be thought of, although the skin and mucous-membrane manifestations would be difficult to interpret on this basis. Since they played so large a part in the clinical picture, I believe this diagnosis is entirely inadequate. The same reasoning can be applied to a consideration of subacute bacterial endocarditis. Since no comment is made regarding blood cultures, I assume that they were negative.

The possibility of dermatomyositis should be considered whenever a diagnosis of systemic lupus erythematosus is under judgment. As Keil<sup>1</sup> has shown, these two diseases may be almost identical clinically. Difficulties in distinguishing between them are usually encountered in patients with

induration of the subcutaneous tissues and muscles, however, and this has not been described in the patient under discussion. The absence of abnormalities of the urine would by itself tend to favor a diagnosis of dermatomyositis as opposed to disseminated lupus erythematosus. Evidence in favor of acute disseminated lupus erythematosus rather than dermatomyositis is more imposing and includes the following: absence of involvement of the eyelids; the occurrence of pericarditis; the apparent absence of any real myositis; the definite enlargement of the lymph nodes; and the occurrence of symptoms referable to the nervous system.

It appears therefore that the probable diagnosis in this case is systemic lupus erythematosus. Since the post-mortem findings in patients dying of this disease are often very few, it is worth while to enumerate those which may be found in this case. The skin lesions, the large lymph nodes and spleen, the pericarditis, possibly with effusion, and the vascular lesions of the central nervous system may well be described. It will be interesting to find if there is gross or microscopic evidence of renal disease, since no urinary abnormalities were noted during life. Endocarditis may or may not have been present. It is quite likely that otitis media was found at death, and there may have been bacterial evidence of terminal septicemia. As has been pointed out in previous conferences here, the final diagnosis must be made by considering the post-mortem findings along with the symptoms and signs present before death.

#### CLINICAL DIAGNOSIS

Acute lupus erythematosus disseminatus.

#### DR. ZELLER'S DIAGNOSES

Acute lupus erythematosus disseminatus.  
Otitis media.  
Terminal septicemia?

#### ANATOMICAL DIAGNOSES

Lupus erythematosus disseminatus, acute.  
Acute endocarditis, terminal (bacterial?).  
Focal necrosis of myocardium.  
Infarcts of spleen, kidneys and brain.  
Otitis media, right.  
Mastoiditis, acute suppurative, right.  
Meningitis, acute.  
Bronchopneumonia, early.  
Pulmonary atelectasis.  
(Chorea.)  
Peritonitis, chemical, from perforation of stomach (probably post mortem).

## PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: As Dr. Zeller has pointed out, the anatomic findings in cases of acute disseminated lupus are often disappointingly few and are at best extremely inconclusive. On the other hand, when the clinical and the anatomic findings are added together, a symptom complex can be built up that is reasonably characteristic. I know of no anatomic finding that is conclusive. Even the skin rash may be very transitory, and no trace of it may be found at the time of death. In this case, it was still present in marked form; otherwise we should have been quite at a loss to make an anatomic diagnosis. A relatively frequent finding in these patients is a polyserositis, but in this case there was no inflammation of the pericardium or pleura and a localized patch of fibrin about the tip of the appendix was all that suggested peritoneal involvement. Enlargement of the spleen and lymph nodes, which is relatively constant, was found in this case. On histologic examination, acute necrosis of the germinal centers was apparent, a very characteristic point in the more acute cases. The heart was normal in size but did show an acute endocarditis of the mitral and aortic valves. From this source, emboli had developed and had produced small infarcts in the spleen and kidneys. The kidneys, furthermore, showed what is called focal glomerular nephritis. By this term we mean findings in occasional glomerular tufts or even in sin-

gle loops of the tufts essentially like those of glomerular nephritis but with many entirely normal glomeruli. This is a frequent finding in disseminated lupus but is also characteristic of subacute bacterial endocarditis, so that in this case it does not serve as a differential point. There was, as was suspected, an acute otitis media and also a mastoiditis on the right. The cerebral symptoms were explained by the presence of a nasal meningitis and also of an early abscess in the right cerebellar lobe. No path of spread of the infection from the mastoid could be made out, so that we do not know whether the cerebellar abscess was secondary to the mastoid or was the result of a septic embolus. Unfortunately no cultures were made of either the endocardial vegetation or of the cerebellar abscess. The character of the endocardial lesion, however, leaves little doubt that the endocarditis was of the bacterial rather than the peculiar nonbacterial type often referred to as Libman-Sacks<sup>2</sup> endocarditis. In summary, it seems probable that we have been dealing with a case of acute disseminated lupus complicated, as these cases not infrequently are, by terminal sepsis, which in this case took the form of a subacute bacterial endocarditis.

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were racially or culturally adapted to their patient clientele, but very few were confronted with a failing supply of interns. The primary concern of most hospitals was to secure and maintain the approval of their institutions as suitable places for young graduates to serve internships. They assumed, or perhaps were led to believe, that such approval would vouchsafe for them a continuing supply of interns. Ten years ago, it did.

Today, the problem has changed. Hospitals in general are less concerned with the qualifications of their interns, although they naturally want the best available, and many of them are even worried by the possibility of being unable to provide a fully staffed intern service. Refugees who cannot speak the English language fluently are in demand, and are actually securing histories from patients who cannot understand their questions. Today, there are in the United States one thousand internships for which there are no interns, and for which there are not likely to be interns for many years to come. The military exigencies facing the Nation are beginning to accentuate this situation, but one should not make the mistake of assuming that they have in any way brought this about: the cause is very plain and should be understood by all who are affected by or interested in the problem.

The annual number of medical-school graduates has changed very little during the past ten years; although there was a 20 per cent increase from 1930 to 1937, the number has again fallen off, so that the 1940 and 1941 figures are approximately identical with the average for the decade. Against this relatively fixed supply, there has been a steadily increasing demand for interns' services by the hospitals. Not only has the number of hospitals seeking to use and to train interns increased, but almost all that had had an intern staff have enlarged it. Hospitals have also increased the number of resident physicians in their employ, and in some institutions it has become a part of the hospital economy to give board and room to third-year and fourth-year medical students in return for their services during the evenings and week ends. Apparently, this list

## INTERN SUPPLY AND DEMAND

Hospital administrators expect to face continual new adjustments as the role of the hospital in medical care and medical education continues to change. The medical and surgical service rendered in the modern hospital has come to depend more and more on the activities of interns—usually, recent medical school graduates who seek to gain practical experience and instruction to supplement their medical education. It gradually evolved that the hospitals and the interns each had a need for the facilities and services of the other, and ten years ago, there appeared to be an approximate balance between these mutual facilities and services in the United States. Some hospitals were then at pains to secure interns who

type of hospital service is the least regulated, and can be utilized by hospitals that do not even apply for approval by the Council on Medical Education and Hospitals of the American Medical Association. This dislocation between supply and demand has been made even more stringent by the steady increase in the amount of laboratory work called for today, as compared with that requested ten years ago. Even when this is accompanied by a corresponding increase in laboratory personnel, the work of the interns is not simplified. Consequently, the hospitals of the United States are now engaged in a new type of competition—a competition for their rightful share of the limited supply of available interns.

Among the hospitals in certain metropolitan areas, regulatory procedures have been in operation for many years. So far as they concerned those areas and so far as they did not involve the fourth-year medical students in too many schools, these regulations worked well; but when one metropolitan area advanced the date of its examinations and stipulated that the students selected must immediately accept the appointments or refuse them forthwith, the next year another area was sure to advance the date again. Last year, it was generally agreed that appointments would not be made before a certain day in November, but many hospitals jumped the date when it seemed to be advantageous for them to do so. This year, at least one hospital has written to some of the medical schools asking for the names and addresses of all students in the upper third of the graduating classes—offering to pay the schools for the compilation of such a list—so that they might circularize these men and perhaps inveigle them in advance of other opportunities or commitments. The competition is becoming keen, and for the fourth-year medical student to be competed for rather than to be in competition is a refreshing situation. He who is being competed for, however, must be wary. He should develop sales-resistance, for he will inevitably be approached, proselyted and attracted by whatever devices hospitals can legitimately employ to secure their share of intern attention and service,

and the institutions that talk the loudest should bear particular scrutiny.

Even if the medical schools could increase their output and thus satisfy the demands for intern service,—which at the present time they cannot do without lowering the standards of medical education,—this merely means that a serious oversupply of practicing physicians would eventually occur, since the very increases in the utilization of hospitals that have brought about the present disproportions have already diminished the practice of domiciliary medicine. Economic laws seem to point toward an arrangement whereby those hospitals that do not or cannot provide bona fide educational privileges to their interns would hire graduate interns as resident physicians, thus adding to the cost of medical care but, on the other hand, staking the fledgling physician to the price of an automobile and his first month's rent or the wherewithal with which to pay his debts when he eventually begins private practice.

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### JOURNAL OF CLINICAL ENDOCRINOLOGY

THE growing field of endocrinology has demanded another journal. In 1917, *Endocrinology* was begun and for many years this important publication, under the direction of the Association for the Study of Internal Secretions, has maintained a high standard of excellence. Papers, however, on the biochemical aspects of the endocrines from highly specialized laboratories have been printed in the same issue with clinical reports. The two aspects of the same problem are, of course, intimately related but may be easily separated without loss to either. Hence, a new journal, the *Journal of Clinical Endocrinology*, published under the same auspices, has been started; it reflects the advances in clinical studies and should prove to be of great use to practicing physicians. The senior publication will continue to report on laboratory investigations and will thus complement the new journal.

The *Journal of Clinical Endocrinology*, begun in January, 1941, with Milton Lee as managing editor and Charles C Thomas as publisher, is a

welcome addition to medical literature. With in editorial committee of distinguished contributors to the field of endocrinology, such as Fuller Albright, J S L Browne, E C Himblen, E L Seyringhaus and K W Thompson, the new journal starts with a sound foundation for a successful career.

## MEDICAL EPONYM

### KLEBS-LOEFFLER BACILLUS

The bacillus of diphtheria was discovered by Edwin Klebs (1834-1913), of Zurich, and reported at the Second Congress for Internal Medicine in Wiesbaden on April 19, 1883. The paper 'Die Diphtherie [On Diphtheria]' is printed in *Verhandlungen des Kongresses für innere Medizin* (2 139-154, 1883). A portion of the translation follows:

In form, these rods are of equal length; they are arranged in a row and on the whole, hardly as large as the bacilli of *A. fur* number are spore bearers, each way having two spores, one at each end.

Friedrich August Johann Loeffler (1852-1915) in a monograph entitled *Untersuchungen über die Bedeutung der Mikroorganismen für die Entstehung der Diphtherie beim Menschen und der Taube und beim Kalbe* [Studies concerning the Significance of Micro organisms in the Etiology of Diphtheria in the Human Being, in the Pigeon and in the Calf], was able to demonstrate by the application of Koch's postulates that the organism described by Klebs was indeed the etiologic factor in diphtheria. In this monograph, which was published in the *Mitteilungen aus dem Kaiserlichen Gesundheitsamte* (2 421-499, 1894), the author refers to previous investigations. A portion of the translation follows:

We thus see that studies dealing with the significance of bacteria that occur in diphtheritic material have not as yet led to any satisfactory conclusions. It seemed imperative, therefore, to attack the solution of this important question with the help of the newest investigative methods, namely Koch's methods of culture on solid media and thus to discover the significance of all these kinds of bacteria. It was necessary, first, to determine which varieties, by reason of their relation to the diseased tissues, seem to be chiefly concerned in the etiology of diphtheria, then to grow these in pure culture, and finally to undertake animal inoculation experiments with the pure cultures in as many species as possible.

There follows a detailed account of the successful investigation that enabled him to say in conclusion: 'We thus have here two examples of perfect, infectious diphtheria of pure bacillary origin.'

R W B

## MASSACHUSETTS MEDICAL SOCIETY

### SOCIETY HEADQUARTERS

Owing to the shortage of fuel oil, the Boston Medical Library will be closed on Saturdays, commencing October 4 and continuing until late spring. This will necessitate the closing of the headquarters of the Society and the office of the Journal during the corresponding period. In an emergency, the officers of the Society and the managing editor and associate editors of the Journal will be available through their offices or homes.

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

#### FATAL FIBROCASEOUS TUBERCULOSIS AND FEMORAL THROMBOPHLEBITIS FOLLOWING CESAREAN SECTION

A twenty four year old primipara entered the hospital at term for an elective cesarean section four hours after the rupture of the membranes. The indication for the cesarean section was a small round pelvis.

The heart and lungs were reported to be normal. The patient was first seen when approximately sixteen weeks pregnant and was followed routinely and adequately.

On admission to the hospital, the temperature was 98°F, the pulse 120, and the respirations 20, when the patient returned from the operating room, the temperature was 101°F, the pulse 92, and the respirations 24. From then until the fortieth postoperative day, when she died, the patient ran a continuous fever,—a temperature of 98 to 103°F,—respirations of 30 to 35, and a pulse of 110 to 120. At some time during the puerperium, a right femoral phlebitis developed. A medical consultant saw the patient and noted that there was evidence of a very rapidly developing miliary tuberculosis. The patient was transfused several times and treated conservatively.

Autopsy showed bilateral fibrocaseous tuberculosis, with extensive cavity formation, and right femoral thrombophlebitis.

**Comment.** It is very hard to understand how such an extensive tuberculous process could have existed during pregnancy without being discovered. The operation was performed solely because of pelvic disproportion, and it was not until the temperature rise called attention to the lungs

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters could be addressed to Dr. Ray and S. T. us Secretary, 350 Dartmouth Street, Boston.

that the pulmonary process was recognized. It is perfectly possible, in fact probable, that an old tuberculous process was lighted up by the infection that followed the cesarean section. Hence, the cesarean section was probably the indirect cause of death. If the infection had not resulted, the tuberculous process would probably have remained not only quiescent but entirely unrecognized.

Tuberculosis is not a common complication of pregnancy. Patients with mild cases under hospital care may go through pregnancy without undue risk, and it is only in advanced cases that fatalities ensue.

#### DEATHS

**CHOLERTON**—HERBERT CHOLERTON, M.D., of West Somerville, died September 25. He was in his sixty-ninth year.

Born in Manchester, England, Dr. Cholerton received his degree from Harvard Medical School in 1901. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

He is survived by his widow, his mother, a sister, and a brother.

**KELLEHER**—PATRICK F. KELLEHER, M.D., of Cambridge, died September 25. He was in his seventy-fourth year.

Dr. Kelleher received his degree from Tufts College Medical School in 1896. He served on the staffs of St. Elizabeth's and Cambridge City hospitals, and was a fellow of the Massachusetts Medical Society and the American Medical Association.

His son and a sister survive him.

**LANE**—EDWARD B. LANE, M.D., of Milton, died September 17. He was in his eighty-second year.

Born in Melrose, he attended Boston University and graduated from Harvard University. He received his degree from Harvard Medical School in 1885 and served his internship at the McLean Hospital, after which he became assistant physician at the Northampton State Hospital. In 1895, he was appointed first superintendent of the Boston State Hospital, a position that he held until 1905, when he retired to private practice.

From 1898 to 1903, Dr. Lane was clinical instructor in mental diseases at the Harvard Medical School, resigning to become professor of mental diseases at the Tufts College Medical School; he retained this position for twenty-five years. He was formerly resident physician at the Adams Nervine in Jamaica Plain. He was a member of the Massachusetts Medical Society, the American Medical Association, the American Urological Association, the American Psychiatric Association and the Dorchester Medical Club.

His widow, three sons and a sister survive him.

**MALLORY**—FRANK B. MALLORY, M.D., of Brookline, died September 27. He was in his seventy-ninth year.

Dr. Mallory received his degree from Harvard Medical School in 1890. He was professor of pathology at the Harvard Medical School for many years and was head of the Pathological Laboratory, —later called the Mallory

Institute of Pathology, —Boston City Hospital, from 1897 until his retirement in 1933. He was a fellow of the Massachusetts Medical Society and the American Medical Association and a member of the American Association of Pathologists and Bacteriologists, having served as its treasurer for many years. Dr. Mallory was the author of two standard pathological textbooks and many original articles, and for fifteen years was editor of the *American Journal of Pathology*.

He is survived by a sister, Miss M. Eleanor Mallory, of Avon Park, Florida, and by two sons, Dr. Tracy B. Mallory and Dr. G. Kenneth Mallory, both of Brookline.

**TOBEY**—GEORGE L. TOBEY, Sr., M.D., of Medonak, Maine, died September 18. He was in his eighty-ninth year.

Dr. Tobey formerly served on the staff of the Clinton Hospital, and had been district medical examiner. He was a former member of the Massachusetts Medical Society, and was a member of the *Maine Medical Association* and the American Medical Association.

His sons, Dr. George L. Tobey, Jr., Dr. Harold G. Tobey, and Guy D. Tobey, survive him.

#### CORRESPONDENCE

##### INFORMATION CONCERNING THE ARMED FORCES IN PHYSICIANS' WAITING ROOMS

*To the Editor:* During the past few weeks, several medical men in New England have informed this headquarters that they would be pleased to take a more active part in the national defense effort. In particular, several physicians have signified their desire to secure accurate information about current opportunities in the United States Army for young men who were their patients or relatives and friends of patients.

In this connection, it has also been suggested that many professional offices would lend themselves most fittingly to the display and possible distribution of reliable information about the armed services in the form of official publications, which might be included with the other standard reading matter of a physician's waiting room.

May I take this opportunity to invite any physician in New England who wishes to join others in this vital phase of national defense to notify the Commanding General, First Corps Area, Army Base, Boston, Attention CARO? Appropriate material will promptly be furnished.

The fine spirit that your profession has already displayed in innumerable ways during the current emergency makes me sure that all its members who find it possible will co-operate in this matter.

F. B. WILBY

*Brigadier General, United States Army*

First Corps Area  
Army Base, Boston

##### PREMARITAL MEDICAL EXAMINATIONS

*To the Editor:* I am much interested in House Bill No. 460 dealing with premarital physical examinations, a transcript of which appeared in the August 28 issue of the *Journal*.

Section 20B states, "If such physician, in making such examination, discovers evidence of any infectious disease declared by the state department of public health to be dangerous to the public health, he shall inform both parties of the nature of such infectious disease and of the pos-



sibilities of transmitting the same to his or her marital partner or to their children. Such examination shall include a standard serological test for syphilis. If either applicant is suffering from one of the more obvious reportable diseases, like smallpox or diphtheria, the physician's problem is relatively simple. But it is quite evident from the demands for a serologic test for syphilis that the intention of the bill is likewise to exclude gonorrheal disease in both applicants.

Shall the physician rest content with a cursory injection of the antenatal phallus, or shall he also make sure the prospective bridegroom's prostate is secure with microscopic evidence of purity of soul and sanctity of habit? And if so, should he be content with aught but cultural evidence of noninfectiousness? And what of the blushing bride? To rest content here with a negative Hinton test and a throat and skin free of obvious infection is hardly to carry out the purpose of this legislation. Are we to certify that the lady is free of infectious disease dangerous to the public health when we have the remotest idea of the existence or character of discharge? And shall we be satisfied with a non-pudendal smear, or must we go into the problem deeply? Here we are faced with a perplexing social taboos and sentimental prejudices.

To imply ridicule of this estimable piece of legislation is farthest from my thoughts, but on the shoulders of every practicing physician has descended a very real responsibility to the State as well as to the patient. How, then, an examination should be performed in order to certify the spirit and the letter of this law and to enable the physician to assert without fear of serious consequence that neither party harbors a reportable contagious disease? Unless frank discussion of this problem prior to some unanimity of opinion and of practice the whole can become a farce that merely creates a sense of insecurity in the minds of the affianced.

ALLEN S. JOHNSON, M.D.

121 Chestnut Street  
Springfield, Massachusetts

## POST PARTUM EMBOLISM

To the Editor: In the August 28 issue of the *Journal* under the Section of Obstetrics and Gynecology of the Massachusetts Medical Society, a case of post partum phlebitis and fatal pulmonary embolism was presented and the assertion was made that death might have been averted had the patient been kept in bed for a longer period. The fever was assumed to have been due to pelvic thrombophlebitis, although no evidence other than fever is given to support this diagnosis. On the other hand, the presence of tenderness in the leg, together with fever, should have been regarded as presumptive evidence of thrombophlebitis of the deep veins in the lower leg.

The assumptions made in that report deserve revision in view of the recent evidence concerning the etiology of pulmonary embolism to wit, that the vast majority of emboli arise from thrombophlebitis of the deep veins of the lower leg; that the treatment of such thrombophlebitis by prolonged rest in bed is not an effective safeguard against the occurrence of embolism; that the existence of an unexplained fever and tenderness in the lower extremity makes it incumbent on the physician to make or dismiss the diagnosis of thrombophlebitis on the basis of x-ray visualization of the deep veins by Bauer's technique, that once the diagnosis is made the only certain prophylaxis against embolism is immediate ligation of the femoral vein proximal to the clot, or heparinization, which is less

desirable for reasons already pointed out by various writers.

In the case referred to it is clear from existing data that keeping the patient in bed for a longer period would not have guaranteed the avoidance of embolism whereas ligation performed in time and in the right circumstances would. Gynecologists and obstetricians should revise their assumption that the site or origin of emboli in their cases is from the pelvic veins. This belief continues to render them helpless to avoid the calamity of embolism. The facts warrant an optimistic view in regard to an effective prophylactic technique against embolism. Careful observation of the lower extremities in post partum and post-operative patients should lead to a sharp reduction in the incidence of fatal pulmonary embolism.

ARNOLD STARR, M.D.

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Boston

## DEFENSE COUNCILS

To the Editor: According to a joint statement issued on September 4 by the director of the Office of Civilian Defense, F. H. LaGuardia, and the chairman of the American National Red Cross, Norman H. Davis, state and local defense councils are the official agencies responsible for the co-ordination of all available resources that may be required for civilian protection in the event of belligerent action. Defense councils should therefore acquaint themselves with the resources of the local Red Cross chapters in providing food, clothing, shelter, nursing care, transportation and other basic necessities and should integrate them into the comprehensive local program. Duplication of trained and experienced personnel and of available supplies of the Red Cross should be avoided except where supplementation is essential to meet the anticipated needs of the community.

GEORGE BAEHR, M.D.  
Chief Medical Officer

Office of Civilian Defense  
Washington, D. C.

## BOOK REVIEWS

*Scabies—Civil and Military Its prevalence prevention and treatment.* By Reuben Friedman, M.D. 8°, cloth, 288 pp. New York: Froben Press, 1941. \$3.00.

The subject of scabies is thoroughly reviewed in this book, particularly in its historical and military aspects. Over two hundred pages are devoted to the importance of scabies in relation to war, but there are also chapters on scabies in Colonial America and similar historical data. The material, in general, is badly presented and the book is difficult to read. Considerable semi-irrelevant or badly digested facts are included. Moreover, the format is unattractive, and in many places there is evidence of lack of care in printing. The book, although it contains some material of interest, is not one that can be enthusiastically recommended.

*Textbook of Medicine.* By various authors. Edited by J. J. Conybeare, M.C., D.M. (Oxon.) F.R.C.P. Fifth edition. 8°, cloth, 1131 pp., with 24 illustrations, and 31 x-ray plates. Baltimore: Williams and Wilkins Company, 1940. \$7.50.

The fifth edition of this book, which was first published in 1929, is an indication of its worth to the medical

profession. Made up of contributions by various authors, but edited by Dr. Conybeare, physician to Guy's Hospital in London, this volume has long maintained an important place in the world of medical textbooks. This edition contains a great deal of new material, for many sections have been partially rewritten and some completely revised. Articles on sulfonamide therapy, blood transfusion, herniation of the nucleus pulposus and similar modern additions to medical knowledge are included. It has not been possible, however, to keep the book strictly up-to-date, largely because of the emergency created by the war in England. The authors are apparently not acquainted with many recent additions to medical literature, although the volume maintains its position as an important textbook.

*Medical Diseases of War.* By Sir Arthur Hurst, D.M. (Oxon.), F.R.C.P., with the co-operation of H. W. Barber, M.D. (Cantab.), F.R.C.P., F. A. Knott, M.D. (Lond.), M.R.C.P., and T. A. Ross, M.D. (Edin.), F.R.C.P. 8°, cloth. 327 pp., with 37 illustrations and 4 plates. Baltimore: Williams and Wilkins Company, 1940. \$5.50.

This book, a new edition of one first published in 1916 and republished in 1918, will be found especially helpful to neurologists and to all interested in the neuroses of war. It is based largely on the author's wide experience in World War I as neurologist to Guy's Hospital, officer commanding Seale-Hayne Hospital for Functional Nervous Disorders and consulting physician to the Salonika Army, but under conditions so far experienced it may not be so applicable in World War II.

When one realizes that almost 6 per cent of the 341,025 discharges of soldiers from the British Army from 1914 to the end of April, 1918, were due to war neuroses, the value of recognizing and treating these cases correctly is evident. Hurst's remarks in Chapter I, "Predisposing Causes of War Neuroses," will repay careful reading. Other chapters are entitled "Hysterical Symptoms in Soldiers," "Hysterical Contractures," "Hysterical Postures and Gaits," "Hysterical Tremors" and "Hysterical Blindness"; they contain numerous brief case records, which are instructive. Many results and cures are almost miraculous.

Of especial interest is Chapter XVI by T. A. Ross, entitled "Anxiety Neuroses of War." Here, in particular, psychotherapy, with explanation to the patient, persuasion and re-education, has worked wonders. The chapter, "Soldier's Heart," is very good; in great measure, this is based on Sir Thomas Lewis's book, published in 1918. The section by H. W. Barber, "Skin Disease in War," is of special value. Medical officers of the rapidly expanding Army of the United States, an army composed of men who are very liable to be infected in crowded barracks, should study this section with care.

The title of this volume is somewhat misleading, since almost half of the book is given over to the neuroses of World War I, and the other half concerns almost entirely a number of medical diseases, such as trench fever, typhoid and paratyphoid fevers, bacillary dysentery, epidemic jaundice and tetanus, all of which promise not to be important in World War II, because conditions are so different from those in 1914-18. One expects to have epidemics and perhaps pestilence, but more probably among the civilian population than among the military forces.

Of great value are the references to the published literature, at the end of each chapter. An index also adds to the general usefulness of the volume. This book can well be recommended to those interested in military medicine.

*Neurology: Lectures for medical students and general practitioners.* By Knud H. Krabbe, M.D. 8°, paper, 387 pp., with 4 illustrations. Copenhagen, Denmark: Einar Munksgaard, 1941. 12 Dan. Cr.

Dr. Krabbe, a well-known neurologist from Copenhagen, has long been a lecturer in the hospital and medical school in that city. He is widely known as a distinguished contributor to the literature on neurology. His lecture notes, slightly expanded and carefully translated, are now published in English, a remarkable contribution from Denmark in a time of great uncertainty, because of the German occupation.

The lectures themselves are effectively compiled, and although they report what must be considered only as routine neurologic information, they are written in a pleasant style, with remarkable completeness of material. The book forms an excellent introduction to the subject and should be widely read in this country by medical students and practitioners. There is a flavor, moreover, of continental neurology, not found in American and English textbooks. One should not look, however, for a complete treatise on the subject. These are introductory lectures, but as such are sound, clear and extremely readable. Seldom has the reviewer met with a book by a foreign author that has pleased him more in its English dress. This volume is highly recommended.

In the May 15, 1941, issue of the *Journal*, the price of this book was incorrectly listed as \$12.00. It should have been Danish crowns, or about \$3.00, which is a reasonable price for an important publication.

*Orbital Tumors: Results following the transcranial attack.* By Walter E. Dandy, LL.D., M.D. 8°, cloth, 168 pp., with 100 illustrations. New York: Oskar Piess, 1941. \$5.00.

Up to comparatively recent times, orbital tumors have been operated on by ophthalmologists, who have used the ordinary orbital approach. With the advent of neurosurgery, it was soon discovered that orbital tumors are often intracranial tumors, with extensions into the orbital space, and thus cannot be entirely removed when operated on through the anterior part of the eye. Nearly 75 per cent of primary orbital tumors are also found in the intracranial chamber. Because of this and also because of the more favorable chance of removing the tumor in the orbital cavity, Dandy advocated the intracranial approach as early as 1921. His point of view has now been widely accepted, and, except for tumors lying in the anterior portion of the right orbit where there is no reason to suspect an intracranial extension, all other tumors of the orbit should be exposed by the neurosurgeon. This, indeed, according to Alan C. Woods, who writes the preface to Dandy's book, has become the routine practice at the Johns Hopkins Hospital. The monograph reports 31 cases, in most of which the tumors were removed by Dandy. The book is finely illustrated, has a good bibliography, and is a splendid example of a small monograph on a single field of neurologic and neurosurgical interest. To neurologists, the book is one of prime importance, and it is hoped that the ophthalmologist, too, will recognize its value.

## NOTICES

### HARVARD MEDICAL SOCIETY

Beginning October 14, the Harvard Medical Society will meet once a month on the second Tuesday of each

month, with the exception of November, at 8 15 p m in the amphitheater of the Peter Bent Brigham Hospital. The program for the October 14 meeting is as follows:

Clinical presentation  
Recent Advances in Experimental Renal Hypertension  
Dr Lewis Dexter

#### JOSEPH H PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston  
Lecture Hall, 9-10 a m

#### MEDICAL CONFERENCE PROGRAM, OCTOBER

Wednesday, October 8—Spleen Facts and fancies Dr William Dameshek.

Friday, October 10—A Routine Office Cardiovascular Physical Examination Dr Samuel A Levine

Wednesday, October 15—A Dental Pediatric Presentation Dr F C McDonald and Dr Leonard Despres

Discussion by Dr Basil G Bibby and Dr Paul Boyk

Friday, October 17—Gastric Ulcer Dr Sara Jordan

Wednesday, October 22—Acne, Hirsutism and Menstrual Disorders Dr C H Lawrence

Friday, October 24—Physical Fitness in Late Maturity Dr Robert T Monroe.

Wednesday, October 29—X ray Demonstration Dr Alice Ettinger

Friday, October 31—The Differential Diagnosis of Hemoglobinuria Dr T Hale Ham

On Tuesday and Thursday mornings, from 9 to 10 o'clock, Dr S J Thannhauser will give a medical clinic on hospital cases

On Saturday mornings, from 9 to 10 o'clock, there will be a presentation, with discussion, of dispensary and district cases

There will be no morning medical conferences the week of November 3, during the meetings of the American College of Surgeons

#### JEWISH MEMORIAL HOSPITAL

The first diagnostic therapeutic conference of the Jewish Memorial Hospital will be held at the hospital 55 Townsend Street, Roxbury, on Thursday, October 9, at 11 a m Dr Reginald Fitz will speak on Heart Disease.

Interested physicians and medical students are cordially invited to attend

#### CONSULTATION CLINICS FOR CRIPPLED CHILDREN

The date of the consultation clinic for crippled children, to be held in Gardner, has been changed from October 10 to October 21. The dates of the other clinics is announced in the September 25 issue of the *Journal* remain unchanged

#### SUFFOLK DISTRICT MEDICAL SOCIETY

During 1941-1942, the Suffolk District Medical Society will hold two meetings, instead of three as in previous years. Both meetings are business meetings. The executive committee may, for business or scientific reasons, announce additional meetings during the coming year

Wednesday, October 22, Boston Medical Library, 8 15 p m "Personal Experiences in Unoccupied France, 1941" Dr Harold C Stuart

Wednesday, April 29 Annual meeting Boston Medical Library 8 15 p m Election of officers Virus Infections of the Central Nervous System Drs Houston Merritt and John H Dingle

#### BOSTON DOCTORS SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will resume rehearsals, under Alexander Thiede, on Thursday, October 9, at 8 30 p m at Station WMEN, 70 Brookline Avenue, Boston. Those interested in becoming members should communicate with Dr Julius Loman, 520 Beacon Street, Boston (KEN 3200 or LON 2155)

#### AMERICAN SOCIAL HYGIENE ASSOCIATION

The American Social Hygiene Association is arranging a dinner to mark the thirtieth anniversary of the announcement of the discovery of salvarsan by Dr Paul Ehrlich. Mrs Ehrlich will be the guest of honor on this occasion. Among the other speakers will be Dr Thomas Parran, surgeon general of the United States Public Health Service. The Honorable Frances Payne Bolton will preside.

The dinner will be held in the Jade Room of the Waldorf-Astoria, on Saturday evening, October 11, at 7 30. Tickets may be obtained from the American Social Hygiene Association, 1790 Broadway, New York City, at a cost of \$3.85, including gratuity.

#### SOCIETY MEETINGS AND CONFERENCES

##### CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, OCTOBER 5

MONDAY OCTOBER 6  
10-11 15 p m Clin copathological conference Dr Bent Brigham Hospital amph theater

TUESDAY OCTOBER 7  
10-10 a m Medical clinic Dr S J Thannhauser Joseph H Pratt Diagnostic Hospital  
12 15-1 15 p m Clin coronecological conference Peter Bent Brigham Hospital amph theater

WEDNESDAY OCTOBER 8  
American Academy of Pediatrics Hotel Statler Boston  
9-10 a m Spleen Facts and fancies Dr William Dameshek Joseph H Pratt Diagnostic Hospital  
12 m Clin copathological conference Cl Thannhauser  
2 p m New England Dermatological Society Massachusetts General Hospital Skin Out Patient Department

THURSDAY OCTOBER 9  
9-10 a m Medical clinic Dr S J Thannhauser Joseph H Pratt Diagnostic Hospital  
American Academy of Pediatrics Hotel Statler Boston  
11 a m Heart Disease Dr Reginald Fitz Jewish Memorial Hospital 55 Townsend Street Roxbury

FRIDAY OCTOBER 10  
American Academy of Pediatrics Hotel Statler Boston  
9-10 a m Routine Office Cardiovascular Physical Examination Dr Samuel A Levine Joseph H Pratt Diagnostic Hospital  
8 15 p m The Heart and Treatment of Dr Alice Ettinger  
Dr Edward L Lurie United States Naval Hospital Chelsea

## SATURDAY, OCTOBER 11

American Academy of Pediatrics. Hotel Statler, Boston.

\*9-10 a.m. Presentation, with discussion, dispensary and district cases. Joseph H. Pratt Diagnostic Hospital.

\*Open to the medical profession.

OCTOBER 9-MAY 14. Pentucket Association of Physicians. Page 473, issue of September 18.

OCTOBER 11. American Social Hygiene Association. Page 559.

OCTOBER 13-24. 1941 Graduate Fortnight of the New York Academy of Medicine. Page 834, issue of May 8.

OCTOBER 14. Harvard Medical Society. Page 558

OCTOBER 14-17. American Public Health Association. Page 579, issue of March 27.

OCTOBER 19-23. American Academy of Ophthalmology and Otolaryngology. Page 350, issue of August 28.

OCTOBER 29-30. New England Postgraduate Assembly. Pages 1111, issue of September 11.

OCTOBER 29-NOVEMBER 1. Association of Military Surgeons. Page 473, issue of September 18.

NOVEMBER 3-7. American College of Surgeons. Page 1111, issue of July 31.

NOVEMBER 5-6. American Conference on Industrial Health. Page 473, issue of September 18.

JANUARY 3. American Board of Obstetrics and Gynecology. Page 473, issue of September 18.

JANUARY 10-11. Forum on Allergy. Page 392, issue of September 4

APRIL 20-24. American College of Physicians. Page 996, issue of June 5.

## DISTRICT MEDICAL SOCIETIES

## BERKSHIRE

OCTOBER 30.

APRIL 30.

## BRISTOL NORTH

APRIL 16. Taunton

## ESSEX NORTH

JANUARY 7. Haverhill.

MAY 6. Lawrence

## ESSEX SOUTH

NOVEMBER 12. Beverly Hospital, Beverly.

DECEMBER 3. Salem Hospital, Salem.

JANUARY 7. Danvers State Hospital, Hathorne

FEBRUARY 11. Lynn Hospital, Lynn.

MARCH 4. Essex Sanatorium, Middleton

APRIL 1. Addison Gilbert Hospital, Gloucester

MAY 13. Annual meeting (place to be announced)

## FRANKLIN

NOVEMBER 11.

JANUARY 13.

MARCH 10

MAY 12. Annual meeting.

Meetings will be held at the Franklin County Hospital at 11 00 a.m.

## HAMPSHIRE

NOVEMBER 5. Veterans Hospital, Leeds, 4:30 and 6 00 p.m.

JANUARY 7. Fitchertown State Hospital, 1:00 and 4 00 p.m.

MARCH 4. Hotel Northampton, Northampton, 4:30 and 6 30 p.m.

MAY 6. Hotel Northampton, Northampton, 8:30 p.m.

## MIDDLESEX EAST

NOVEMBER 12.

JANUARY 28.

MARCH 18.

MAY 6.

All meetings will be held at 12.15 p.m. at the Bear Hill Golf Club, Stoneham, except that of May 6, which will be held at Woburn at 6 30 p.m.

## MIDDLESEX NORTH

OCTOBER 29.

JANUARY 28.

APRIL 29.

## NORFOLK SOUTH

NOVEMBER 6.

DECEMBER 4.

JANUARY 8.

FEBRUARY 5.

MARCH 5.

APRIL 2.

MAY 7.

All meetings will be held at 12:00 noon at the Norfolk County Hospital, South Braintree, with the exception of that of February 5, which will be held at the Quincy City Hospital, Quincy.

## PLYMOUTH

OCTOBER 16. Moore Hospital, Brockton.

NOVEMBER 20. Plymouth County Hospital, South Hanson.

JANUARY 15. Brockton Hospital, Brockton.

FEBRUARY 19. Jordan Hospital, Plymouth.

MARCH 19. Goddard Hospital, Brockton.

APRIL 16. Bridgewater State Farm, Bridgewater.

MAY 21. Lakeville Sanatorium, Middleboro.

## SUFFOLK

OCTOBER 22. Page 559.

APRIL 29. Annual meeting. 3:15 p.m., Boston Medical Library

## WORCESTER

OCTOBER 8. Rutland State Hospital, Rutland.

NOVEMBER 12. Grafton State Hospital, North Grafton.

DECEMBER 10. Worcester City Hospital, Worcester.

JANUARY 14. St. Vincent Hospital, Worcester.

FEBRUARY 11. Worcester State Hospital, Worcester.

MARCH 11. Memorial Hospital, Worcester.

APRIL 8. Hahnemann Hospital, Worcester.

MAY 13. Annual meeting, Worcester Country Club, Worcester

## WORCESTER NORTH

OCTOBER 22. State Hospital, East Gardner.

JANUARY 28. Leominster Hospital, Leominster.

APRIL 22. Fitchburg Hospital, Fitchburg.

JULY 22. Henry Heywood Memorial Hospital, Gardner.

## BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

*The Care of the Aged (Geriatrics).* By Malford W. Thewlis, M.D., attending specialist in general medicine, United States Public Health Hospitals, New York City, attending physician, South County Hospital, Wakefield, Rhode Island, and special consultant, Rhode Island Department of Public Health. Third edition, entirely rewritten. 8°, cloth, 579 pp., with 50 illustrations. St. Louis: The C. V. Mosby Company, 1941. \$6.00.

*Effective Living.* By C. E. Turner, Sc.D., Dr.P.H., professor of biology and public health, Massachusetts Institute of Technology; and Elizabeth McHose, M.A., director of physical education for girls and chairman of the Health Council, Senior High School, Reading, Pennsylvania. 8°, cloth, 432 pp., with 164 illustrations. St. Louis: The C. V. Mosby Company, 1941. \$1.90.

*Clinical and Experimental Investigations on the Genital Functions and Their Hormonal Regulation.* By Bern hard Zondek. 8°, cloth, 264 pp., with 59 illustrations and 44 tables. Baltimore: Williams and Wilkins Company, 1941. \$4.50.

*Studies from The Rockefeller Institute for Medical Research.* Reprints, Vol. 118. 4°, paper, 628 pp., with 141 illustrations, 20 plates, 80 tables and 18 charts. New York: Rockefeller Institute for Medical Research, 1941. \$2.00.

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## THE OPEN SAFETY PIN\*

### A Consideration of Its Peroral Removal from the Upper Air and Food Passages

LAMAR G. RICHARDS, MD†

BOSTON

AS APPLIED to a peroral foreign body, there are few greater misnomers than the term "safety pin." So far as its presence in the upper air or food passages is concerned, this type of pin is at once one of the most dangerous and frequent objects to gain accidental access to these regions. The danger arises primarily from the fact that in most cases the pin tends to enter the pharynx or larynx with the point unguarded and held at a wide angle by the spring, thus presenting a hazardous situation in which the delicate walls of the upper air and food passages are subject to pressure and possible perforation by the point of the pin. The frequent occurrence of such accidents is due to the almost universal use of the safety pin in dressing infants—an age group in which this type of foreign body is most frequently seen. In spite of constant medical admonition, mothers and attendants continue to leave safety pins open and with unprotected points within easy reach of babies whose natural instinct is to put them in the mouth. Added to this is the bad example so often set by mothers themselves in holding such pins in the mouth, with the inevitable result that youngsters tend to imitate this indiscretion. Occasional accidental swallowing of the pin by an adult may result from this pernicious habit.

I believe that this situation warrants closer attention from the pediatrician and the general practitioner, who will so frequently be the first to see such patients. For this reason I am presenting some conclusions drawn from personal experience with regard to clinical observations and secondary to the operative technic involved in the peroral removal of these foreign bodies.

In a recent article, Clerf<sup>1</sup> reports that of over 825

foreign bodies removed endoscopically, 77 were safety pins. In 59 cases, or 77 per cent, the pin was removed from the food passages, in the remaining 18 it had lodged in the air passages. In a personal series of over 150 peroral foreign bodies, 25 have been some form of safety or clasp pin, 90 per cent of which were in the food passages.

Because of this experience with the removal of such pins from the upper air and food passages, I have come to believe that no specific operative technic is applicable in all cases. Chief consideration must be given to the location of the pin and the relation of the point to this location. As an aid in the visualization of the commonest sites of pin lodgment, there is reproduced in Figure 1 a group of photodiagrammatic x-ray films to show representative situations within which, with slight variations, will fall almost all open safety and clasp pins that accidentally find their way into the air and food passages. Divergencies from these typical positions will of course occur, but slight differences of a centimeter above or below the midesophageal region or a minor tilting of the pin to the right or left has no essential bearing on satisfactory methods of removal later to be discussed. These representative positions will first be considered individually.

#### LOCATION OF PIN

##### *Hypopharynx*

It is in the hypopharynx (Fig 1A), particularly in infants up to the age of one year, that one finds over 50 per cent of all open safety pins. The point is usually upward either to the right or to the left and most frequently buried, at least at the termination of the shaft, in the mucosa of the lateral pharyngeal wall. In this position, the spring is resting just at the mouth of the esophagus and occupies the somewhat narrow constriction known

\*From the Bro. Joseph Clinic, Massachusetts Eye and Ear Infirmary.  
†From Boston Mass. House of Eye and Ear Infirmary.

as the cricopharyngeal ring formed by muscle fibers that, attached to the posterior surface of the cricoid cartilage, are embedded in the lateral and posterior surfaces of the constrictor muscles. This muscular ring exerts a somewhat sphincterlike action and is recognized as a line of demarcation or boundary with respect to any esophageal foreign body, depending on whether such objects

The relation of the plane of the pin to that of the hypopharynx is of almost pathognomonic significance. Any pin in the hypopharynx will appear, in a true anteroposterior roentgenogram, in its full expanse, with but little if any foreshortening, as shown in Figure 1A. For this reason, in a true lateral view, the pin will be seen from the side and hence will show no evidence of details

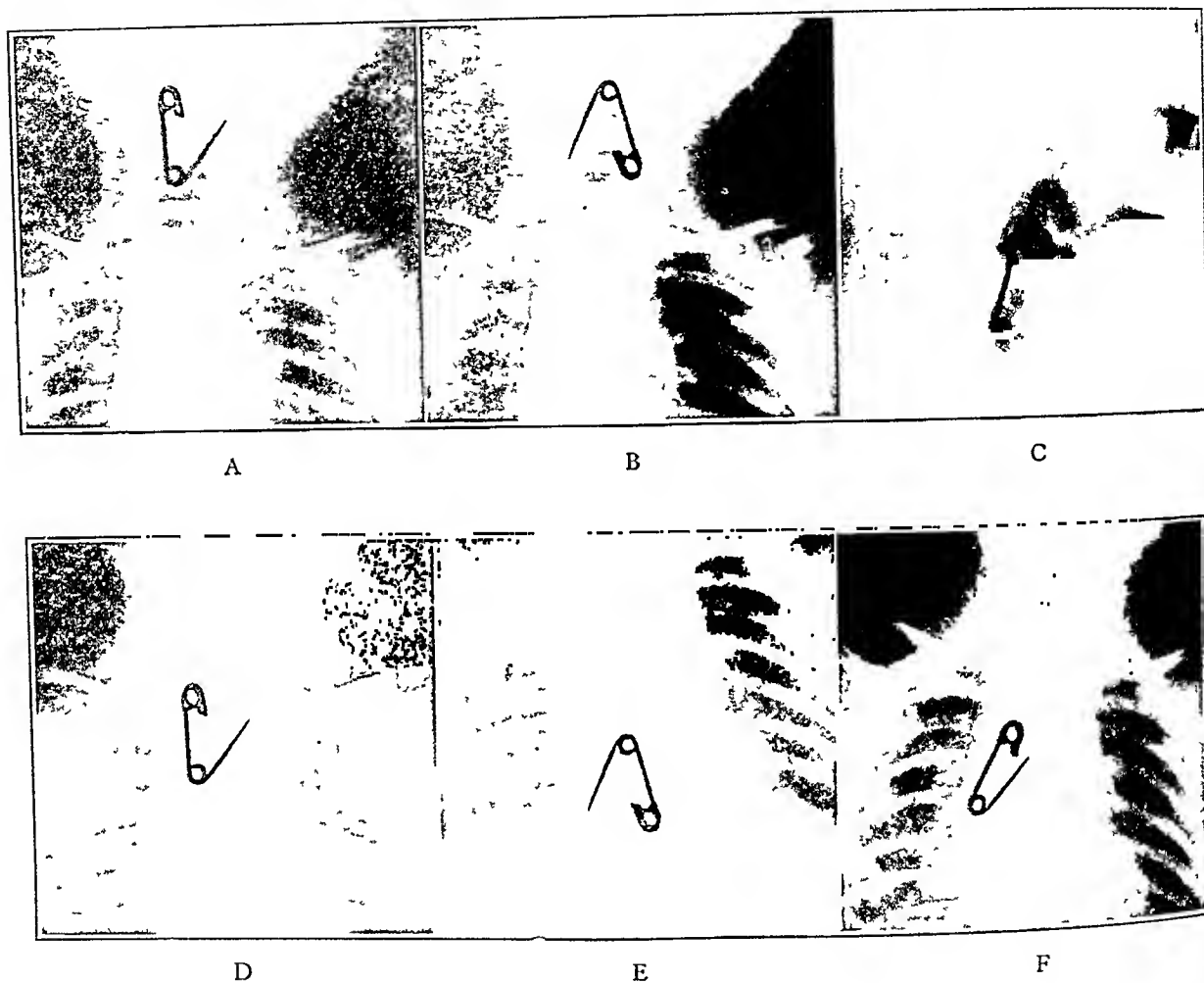


FIGURE 1. *Photodiagrams of Open Safety Pins in Representative Positions in the Upper Air and Food Passages.*

A—hypopharynx, point up; B—hypopharynx, point down; C—larynx, point up; D—esophagus, point up; E—esophagus, point down; F—right bronchus, point up. An intentional disproportion between the size of the pin and the roentgenogram has been employed for purposes of illustration.

are above the cricopharyngeus muscle or below it. This differentiation, as will be seen later, is of the greatest importance in selecting the method of removal best suited to the individual case. The keeper of a pin in the hypopharynx is usually found at a slightly higher level than the point, but slight changes in angulation may leave both keeper and point on a horizontal line. Most frequently, the keeper shaft of the pin will be in a vertical position, the pointed shaft assuming an angulation with the vertical dependent on the degree to which the pin is open.

of expansion or relation of point and keeper to each other. Since an absolutely uniform lateral exposure is difficult to secure, there will, in this exposure, frequently be a slight divergence between the two shafts, but this appearance is quite distinct from that seen when the pin is lodged in the larynx (Fig. 1C).

Lodgment of a pin in the hypopharynx depends somewhat on its size. The larger the pin, the greater the spread at the spring and the less likely it is, particularly in young children, to pass deep into the upper esophagus. In spite, however,

of any relatively high roentgenologic appearance, it is only rarely that the pin can be seen on direct inspection of the throat. When this is possible on forceful depression of the tongue, the top of the keeper may be glimpsed, a point of importance only if x-ray facilities are unavailable or yield negative results.

Far less often a pin in the hypopharynx comes to rest point downward (Fig. 1B). This position is at once recognizable roentgenologically, the pin still assuming its typically transverse relation in the anteroposterior view.

### *Larynx*

It is Nature's intention that any appropriate object put in the mouth shall be swallowed, passing into the esophagus and thence into the stomach. To this end, a complicated and beautifully co-ordinated series of muscular movements propels the object along the proper course. For this reason, more than 90 per cent of all open pins that find accidental lodgment in a child's throat are found in some part of the alimentary tract—hypopharynx, esophagus or stomach. During the act of swallowing even so awkward an object as an open safety pin, there takes place a temporary closure of the larynx or gateway to the upper air passages, which prevents any foreign substance from gaining access to this vital and sensitive region. Only occasionally, in an unguarded moment, can a foreign object near the orifice of the larynx, during a deep inspiration provoked by laughing, coughing or crying, evade the swallowing guardian and so be drawn into the upper airway. This situation, which the layman interprets as "swallowing the wrong way," causes such small objects as nut fragments, tacks and other bits of hardware to reach the tracheobronchial tree.

This same explanation accounts for the occasional lodgment of an open safety pin in the larynx (Fig. 1C). Since the diameter of the latter is much less than that of the hypopharynx, it is quite understandable why a pin of any except extremely small size meets obstruction to further advance and therefore, fortunately, fails to enter the trachea. Again, as in the hypopharynx, almost all such open pins in the larynx come to rest with the point upward but with the fundamental and diagnostically significant difference that the pin lies in the sagittal plane. Therefore, a view of its details in the plane of expansion is seen only in lateral roentgenograms of the neck. In an anteroposterior film, there appears usually only a single or closely approximated double shadow, and even this is obscured by the density of the cervical spine directly behind it. The assumption of such a position by an open pin in the larynx is owing to the fact that whereas the greatest width of the

pharynx and esophagus is in the frontal plane, that of the larynx is in the sagittal plane, and only by conforming to this plane can any appreciable part of the pin pass between the vocal cords. It is at once obvious that this fixed relation of the pin to the plane of the food passage or airway is of the utmost diagnostic value in determining the location of the foreign body. More commonly, an open safety pin enters the larynx with the pointed shaft anteriorly, the point itself protruding either just above the cordal junction in the anterior commissure or just beneath this point and hence below the cordal junction. Depending on the size of the pin, the keeper will occupy a position above or between the arytenoid cartilages, in either event resting against the interarytenoid fold in the midline. Only very rarely will such an open pin enter the larynx point downward, when it will still assume the characteristic anteroposterior plane and will be seen in its expanded position only in the lateral film.

### *Esophagus*

It is in their lodgment in the esophagus proper (cervical, upper thoracic or lower thoracic) that open safety pins create the greatest hazard to the patient and the greatest endoscopic problem for the bronchoscopist. Once the pin has passed the sphincter of the cricopharyngeus muscle, it comes to rest in some portion of the esophagus, most commonly in the region illustrated in Figure 1D. Variations somewhat above or below this representative point have no special bearing on the problem of removal and are dependent on such extraesophageal relations as the crossing of the left main bronchus or pressure from the arch of the aorta. So long as such pins do not pass promptly into the stomach, they call for endoscopic removal, and the assumption that they will pass spontaneously is unwarranted by experience. Here again, as in the hypopharynx, the pin will assume its characteristic frontal plane, its detailed relation being clearly evident in anteroposterior roentgenograms.

By far the greatest number of such esophageal pins are found point up. When the reverse is true, there is always a strong suspicion that the pin, advancing spring downward, actually entered the stomach, being subsequently regurgitated back into the esophagus and lodging this time with the point downward (Fig. 1E). Only in cases of extremely small baby safety pins in older children or adults would it normally be possible for an open safety pin to advance to the midesophagus through the constricting cricopharyngeus muscle while maintaining the point in advance.

### *Main Bronchus*

It requires no knowledge of peroral endoscopy to appreciate the hazards to the patient and technical difficulty of removal of an open safety pin lodged in the main bronchus, the rarest of locations, particularly if point up (Fig. 1F). As a rule, only rather small pins can, through sheer impossibility of passing the larynx, reach the lower bronchial tree, barring always the occasional misfortune of dislodgment from the larynx during attempted removal from the latter. The angular spread of any open pin in the bronchus must of necessity be limited, since the bronchial diameter automatically precludes wide angulation.

### *Stomach*

Finally, open safety pins not infrequently are first discovered to be in the stomach, having, through Nature's providence, passed without accident through the esophagus. Whether, once arrived in this temporarily safe harbor, such pins merit endoscopic extraction is a matter of experience, individual judgment and meticulous study of the subsequent clinical course, and constitutes a subject best discussed in connection with the considerations of removal.

### DIAGNOSIS

It is self-evident that the proper treatment of any patient harboring an open safety pin in his air or food passages presupposes a diagnosis of its presence. Consideration must first be given to a history of ingestion or aspiration, or at least of an opportunity for this. In most cases, such a history must come from the parents, almost always the mother or an attendant, less frequently from an older child. Infants or small children can obviously afford no help in such a situation. It is interesting to note that a positive and volunteered story of the swallowing of an open safety pin is much oftener available than that of nuts aspirated into the bronchus, for example. In a personally observed series of 40 cases of such aspirated nuts,<sup>2</sup> the proportion of delayed diagnosis and prolonged sojourn of the foreign bodies before removal was far higher than that of open pins. This fortunate circumstance results, in all probability, from the fact that most persons caring for infants and young children have a fairly accurate idea of the number of pins customarily used in dressing them and of their whereabouts during any moment of changing or undressing. If, during an unguarded moment, the infant procures such a pin, puts it in his mouth and swallows it, it is quite likely that the pin will be missed and a prompt search made for it. With failure to find it, suspicion is very apt to arise that

the child has swallowed it. If, at the same time, there are any such untoward signs or symptoms as coughing, gagging, choking and vomiting, the possibility is likely to be still further considered and a physician called. Apparently, perhaps as the result of greater publicity, parents today seem much more conscious of pins than of such a foreign body as a peanut, with which, as evidenced by the above-mentioned series of 40 cases, the time interval between aspiration and bronchoscopic removal is much longer.

Another factor operating to effect prompt recognition of a safety-pin accident is the age of the patient. In a high percentage of cases, this is less than one year, hence patients have not the freedom to come and go and so, of their own accord, to put other foreign objects in their mouths. In the group aspirating some form of nut, the average age of the patient was over three years, obviously precluding a parental supervision comparable to that of infants under a year of age. Nevertheless, there have been patients who have swallowed or aspirated open pins in whom there was no history of the accident and in whom symptoms caused by the pin were, for an unfortunate period of delay, attributed to some more humble cause. The following case, seen at the Bronchoscopic Clinic of the Massachusetts Eye and Ear Infirmary for removal of an open safety pin from the larynx, clearly illustrates this point.

R. N., a 7-year-old boy, previously perfectly well, while attending school suddenly choked, coughed and vomited. Sent home by the teacher, he immediately reported to his grandmother that he had swallowed a safety pin. She, being quite hard of hearing, failed entirely to grasp the significance of this story. On the return of the boy's mother, she found him quite hoarse and, presuming him to have a cold, summoned a physician. For the ensuing 2 weeks the boy was treated by three physicians for laryngitis, since he advanced no further information about the pin. The latter was only discovered when, after 3 weeks from the date of accident, a fourth consultant suggested an x-ray, which clearly showed the open pin in the larynx. The pin was removed by the method described below.

It is thus apparent that any physician called in such an accident must at least keep the possibility of foreign body, uncommon as it may be, in mind as a cause for sudden, unexplained deglutitory or respiratory distress. It is at least important, so far as infants and safety pins are concerned, to inquire whether a pin is missing, if such information is not previously volunteered. To this point of suspicion on the part of the attending physician, I have called especial attention in discussing accidental inhalation of nuts.<sup>2</sup> Fortunately, an x-ray film is an infallible diagnostic aid in determining the presence of an open safety pin, but its use must be preceded by the thought that a



foreign body may be present. In spite of this, numerous cases are on record in which one and sometimes more than one open pin have remained unrecognized in the esophagus, the symptoms being attributed to some gastrointestinal disturbance, and no consideration given to the true cause of the trouble.

With respect to pins in the air passages, as exemplified by the case cited above, hoarseness is an almost invariable accompaniment of a safety pin in the larynx, since the presence of the pin prevents accurate apposition of the vocal cords. If, however, the pin chances to reach the bronchus, the clinical course may be essentially asymptomatic, except for a slight cough. In both the larynx and the bronchus, respiratory obstruction is not usually a marked symptom. The actual encroachment on the airways by such a pin even in the larynx is not great, and strange as it may seem, the surrounding inflammatory reaction provoked by the presence of the intruder may be very slight. This is in marked contrast to the reaction to the presence of a nut in the bronchus, in which, besides acting as an obstructing ball valve, it is apt to set up a severe and aggravating inflammatory reaction, tending to occlude the airway completely.

Knowing of or suspecting the presence of an open pin in the throat, parents and physicians should, above all, refrain from any crude or traumatizing attempts to remove it. Such efforts will only succeed either in driving the pin still deeper in the throat or possibly in inflicting severe trauma to vital structures. This warning is given, notwithstanding the following letter received on the occasion of a previous similar and public admonition:

I was reading your lecture. When my girl was two years old she got a tin whistle in her throat. I was all alone so took her across my lap and shook and rubbed her. The whistle came across the floor. My doctor said I saved her life. My aunt's brother got a safety pin in his throat, open. She took a buttonhook and saved him. I would do the same thing again to my two grandsons today. You have to use what help is near.

A GRANDMOTHER OF THREE

Once the diagnosis of the presence of an open pin in the hypopharynx, larynx or esophagus has been made, the patient should be referred to some institution adequately equipped for the safe removal of such potentially dangerous foreign bodies.

#### REMOVAL

It has already been stated that methods for the removal of open pins in the air and food pas-

sages must be selected according to the particular problem in hand. Jackson,<sup>3</sup> in a recent textbook, lists sixteen different possible technics for removing safety pins. It is manifestly impossible for an endoscopist working in any but the largest endoscopic clinic to be master of such a multiplicity of procedures, and it has been my experience that in almost all cases reliance on a much smaller number of maneuvers, thoroughly studied and frequently practiced on a manikin or in the surgical laboratory, yields satisfactory results. Unquestionably, very unusual situations require specialized variations in technic, but the description of the following methods will, it is believed, prove adequate as a guide for removing the great majority of open safety pins encountered over a considerable period.

Preliminary to any attempt at removal, it is imperative to make a most careful roentgen-ray study of the patient, clearly establishing the locality of the pin and its relation to anatomic structures. From this study, it should be possible to ascertain, in comparison with a graded series of standard pins, the size of the pin in question. Still more helpful, if available and dependable, is an exact duplicate of the pin brought in by the parent or patient.

#### Anesthesia

The question of anesthesia has long provoked controversy and disagreement among leading endoscopists. Jackson,<sup>3</sup> backed by a wealth of experience, has persistently been an advocate of the policy of giving no anesthesia to children and only local anesthesia to adults. The merits of the various forms of anesthesia available for all endoscopic procedures are beyond the scope of this paper. It has been my experience, so far as the removal of an open safety pin is concerned,—particularly in the esophagus and in infants and very small children,—that there are more advantages than disadvantages accruing from the use of a general anesthetic. With foreign bodies in the larynx and in any patient in whom there is a question of respiratory embarrassment, I should counsel the avoidance of any form of general anesthesia. Otherwise, with appropriately sized instruments, with a competent anesthetist, and with the exercise of utmost gentleness of manipulation, I believe that the resultant relaxation of the esophageal musculature is an advantage that far outweighs any objection to general anesthesia.

#### Pins in the Hypopharynx

*Point down.* In the few cases in which the pin lies point down in the hypopharynx, the mechanical problem should not afford difficulty. Either

a laryngoscope or a small-sized esophageal speculum is used to expose the lower portion of the hypopharynx. The spring of the pin is viewed under direct vision and grasped with alligator forceps, preferably one in which the tips of the jaws carry a small projection. When these projections close over the spring of the pin, they do not fix it but permit it some latitude in lateral rotation, or what may be termed "togglng,"

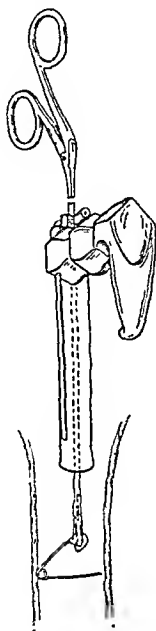


FIGURE 2. *Method of Extraction from the Hypopharynx.*

*The keeper of the pin is grasped; this allows the pointed shaft to follow the line of least resistance.*

at the same time avoiding any tendency for an insecure grasp with possible slipping off of the pin. This togglng permits the pin, during withdrawal, to adapt itself to the pharyngeal wall and thus to find its way with the minimum of resistance. With the point always trailing, no trauma to the pharyngeal walls should occur.

*Point up.* In this position, it is folly to conclude that direct traction, unaided by laryngoscopy, is safe, even when the keeper is easily visible on inspection by direct depression of the tongue. The possibility that such traction will drive the pointed shaft into the pharyngeal wall must never be lost sight of, particularly traction applied without the aid of the laryngoscope and by the simple expedient of grasping the keeper with a curved hemostat.

There are in general two safe and feasible endoscopic methods applicable for pins in the hypopharynx with the point up. In the first procedure (Fig. 2), the keeper, usually the first portion of the pin seen on direct inspection with the laryngoscope or small esophageal speculum, is

grasped through the central lumen with the togglng type of forceps, great care being taken that the teeth of the forceps meet within the eye of the keeper and do not grasp either the distal or proximal margins. Gentle traction is then made, allowing the pin to rotate to the side opposite the point until the pointed shaft occupies a transverse position across the mouth of the hypopharynx. This location tends to occur because the point remains in contact with the hypopharyngeal wall and so acts as a pivot on which, because of the togglng action, the remainder of the pin turns. So long as the length of the pointed shaft does not exceed the width of that portion of the hypopharynx in which it lies, the pin may then be withdrawn without risk of further penetration of the pharyngeal wall by the point. No pressure should be made by the exposing laryngo-

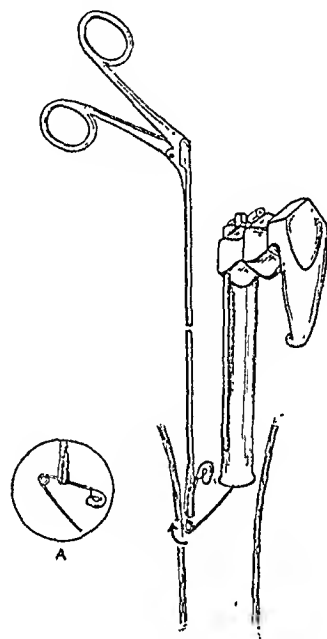


FIGURE 3. *Method of Extraction from the Hypopharynx.*

*The lower end of the keeper shaft is grasped; this allows the pin to rotate. The tip of the laryngoscope guards the point. A — position of pin after "version."*

scope against any portion of the pin that must remain free to assume any position it seeks.

A modification of this method is applicable to pins in the hypopharynx that are of more than average size when it is believed that the pointed shaft might have difficulty in passing out through the pharyngeal diameter or when the pointed shaft is found deeply embedded in the mucosa or musculature of the pharyngeal wall. The shaft of the keeper is exposed to direct vision as far down as possible, preferably even as far as the spring (Fig. 3). An alligator forceps is then introduced parallel to and beside the laryngoscope,

but not passing through the lumen lest it obstruct the view of the exposed shaft. The latter is then grasped as close to the spring as possible and traction made laterally and upward, to displace the spring to the side of the hypopharynx away from the pointed shaft. At the same time, an effort is made to advance the lip of the laryngoscope in close proximity to the pointed shaft, and to hold it in contact with the latter as near the point as its engagement in the mucosa will permit. Thus, the lip of the laryngoscope tends to act as a fulcrum and also as a hindrance to any further advance of the point. With lateral and upward traction with the forceps, the

perfect, if possible, a reasonably satisfactory method and so to practice it in the laboratory as to render it dependable except, perhaps, on the rarest occasions.

For the last fifteen years, it has been my practice with pins in this region to make use wherever possible of the Mosher safety-pin closer. The original model of this highly ingenious instrument has well stood the test of time and in my hands is easier to manipulate than the later and presumably improved variations. Barring minor changes in the obliquity of the distal end and lighting equipment, I can see no reason to alter it. Its use depends on the principle of ad-

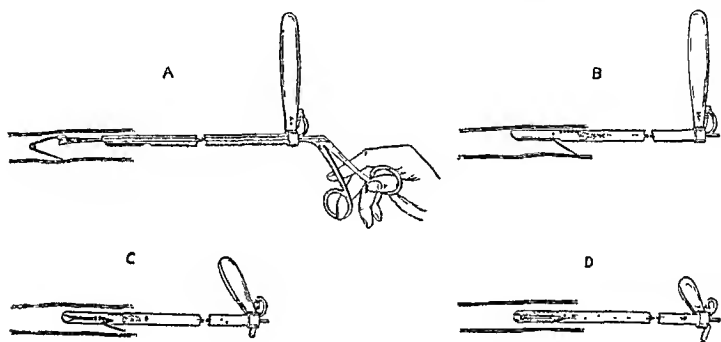


FIGURE 4. Method of Extraction from the Midesophagus.

A—the pin is grasped with toggle forceps passed through a Mosher pin closer; B—the Mosher closer is passed down over the keeper shaft until the spring reaches the transverse slot; C—the closer is rotated preparatory to pushing the pin downward with the pointed shaft impinging on the transverse slot, D—the pin is enclosed in the keeper and held by forceps ready to be withdrawn with the closer and forceps as a unit.

pin swings through an arc, the center of which is the edge of the laryngoscope. Thus is effected what Jackson<sup>3</sup> terms a "version" of the pin to the degree that the previously advancing point becomes converted into a trailing one, permitting ultimate safe removal by the spring or a point on the keeper shaft close to it (Fig. 3A). Once this method of fixation and traction is initiated, there must be no change in the relation of the laryngoscope or forceps lest this distort the mechanical principle and result in possible trauma.

#### *Pins in the Cervical and Thoracic Esophagus*

It is in the removal of open safety pins from this region that one encounters the greatest variability in technic employed by different operators and the expression of amazing ingenuity in the invention of specialized instruments. It is particularly for this reason that it seems wise to

vancing the lower end of the instrument over the keeper and keeper shaft of the pin, while the extended and angulated pointed shaft remains outside and slides through a narrow slot extending somewhat over 2.5 cm. from the distal end of the tube. The proximal end of this longitudinal slot joins a wider triangular-shaped and much shorter lateral slot. Since the keeper of the pin has first been securely grasped with forceps applied under direct vision through the tube and held fixed in this position, without the slightest traction, there is no tendency for the pin to move (Fig. 4A and B). As soon as the point of union of the longitudinal and transverse slot reaches the spring, further advance of the tube is stopped, and the entire tube—but not the forceps—is so rotated as to bring the transverse slot in contact with the pointed shaft of the pin (Fig. 4C). With the tube fixed in this new position, the forceps,

still grasping the keeper, is advanced, forcing the latter downward into the distal portion of the tube and at the same time pushing the pointed arm of the pin against the lower margin of the transverse slot. This results in forcing the pointed arm into the tube until, with further advance of the forceps, the entire pointed arm is sheathed within the tube and the point thus completely protected (Fig. 4D). It is in no way essential that this closure result in the actual entrance of the point within the lips of the keeper of the pin itself. So long as none of the point extends beyond the tube, it is sufficiently protected. The entire system—pin, forceps and tube—in this new relation may then safely be withdrawn through the mouth.

The following fundamental precautions must be rigidly observed if this method is to succeed:

The diameter of the tube or Mosher esophagoscope must be adequate to admit freely the keeper of the pin. Only if this is possible can the maneuver be executed. For this reason, it is of paramount importance to determine the size of the pin with which one has to deal. It is desirable but not imperative that the blades of the forceps permit toggling of the keeper, since it is thereby somewhat easier for the pointed shaft to find its way into the longitudinal slot.

Under no circumstances, once the keeper is thus secured, should any traction be made with the forceps. Unconsciously to make such traction while the esophagoscope is being advanced over the keeper is to risk perforation or penetration of the esophageal wall by the pointed shaft, a far more serious accident with pins in the esophagus than with those in the hypopharynx.

Care must be taken in the final advance of the forceps that the pin is not pushed so far down toward the distal end of the tube that the pointed shaft is permitted to escape from the end. In this event, all the work must be repeated. The moment that the spring appears beyond the tube end, further forceps advance must stop, since the point will already be adequately sheathed. It is in the method of determining the limit of the forceps' advance that one comes to the final and, in many ways, most important requisite, the fluoroscope. I am convinced that fluoroscopic control is absolutely essential in the execution of this method of safety-pin removal from any portion of the esophagus below the cricopharyngeus muscle. Sheathing can undoubtedly be accomplished without this aid, but the added safety is a factor that, I believe, goes far toward assuring success. The

best calculated and positive manipulation in the esophagus can sometimes go awry, and there is no better way to avoid such mischances than the utilization of the help from a competent radiologist, who can observe every technical step in the removal of an open safety pin by this method. At the Bronchoscopic Clinic of the Massachusetts Eye and Ear Infirmary, it is an inflexible rule that all such and many other esophageal and bronchial foreign bodies be removed under fluoroscopic guidance.

Even under the most favorable circumstances and with every possible help, it may not always prove feasible to adhere to the determination to remove an open safety pin through the mouth, even though it is admitted that it entered by this route. If, for any reason, the sheathing method does not proceed to a successful termination, it may be advisable to advance the pin to the stomach and there deposit it. This involves putting one's pride in one's pocket and a chagrining although perhaps only temporary loss of face. A foreign body in the stomach and an untraumatized esophagus are far better for the patient than peroral removal and subsequent mediastinitis. It is the opinion of most general surgeons that an open safety pin in the stomach, if not of undue size, will pass harmlessly through the remainder of the digestive tract without the necessity of any surgical intervention. Unquestionably, it may at times be necessary to remove from the stomach an open pin that, after a reasonable delay, refuses to pass through the pylorus, but this circumstance in my experience has been rare. Such pins in the stomach will not infrequently be found in the stool within twenty-four to forty-eight hours.

For those who dislike such deposition of the pin in the stomach, there is available the method of gastric version in which the pin, grasped by the spring from above, is carried into the stomach, allowed to reverse its position and then brought out, point trailing, through the mouth. With this method, I have had no clinical experience.

The foregoing description of sheathing an open safety pin applies quite obviously to those cases in which the pin rests point up. With the point downward in the lower esophagus, the problem is simpler, involving exposure of the spring by means of the esophagoscope, the grasping of the spring with forceps, preferably toggling, and the withdrawal, at least to a partial extent, of the spring into the lumen of the tube. Here again, although not indispensable, fluoroscopic guidance may be more valuable than one might at first suppose.

### is in the Respiratory Tract

*The larynx.* As already explained, an open safety or clasp pin lodges oftenest in the larynx, point . . . If the point itself is clearly visible above the . . . of the vocal cords in the anterior commissure, it is usually not difficult to grasp the keeper with alligator forceps passed through the laryngoscope and to slip the pin upward without engag-

firmly near the base of the epiglottis and presumably just above the pointed end of the pin (Fig. 5B). With the laryngoscope thus fixed, traction is made on the keeper, which is then withdrawn through the lumen of the laryngoscope, in the process of which the normal acute angulation of the shafts is expanded into a wide, obtuse angle or almost into a straight line (Fig. 5C). This

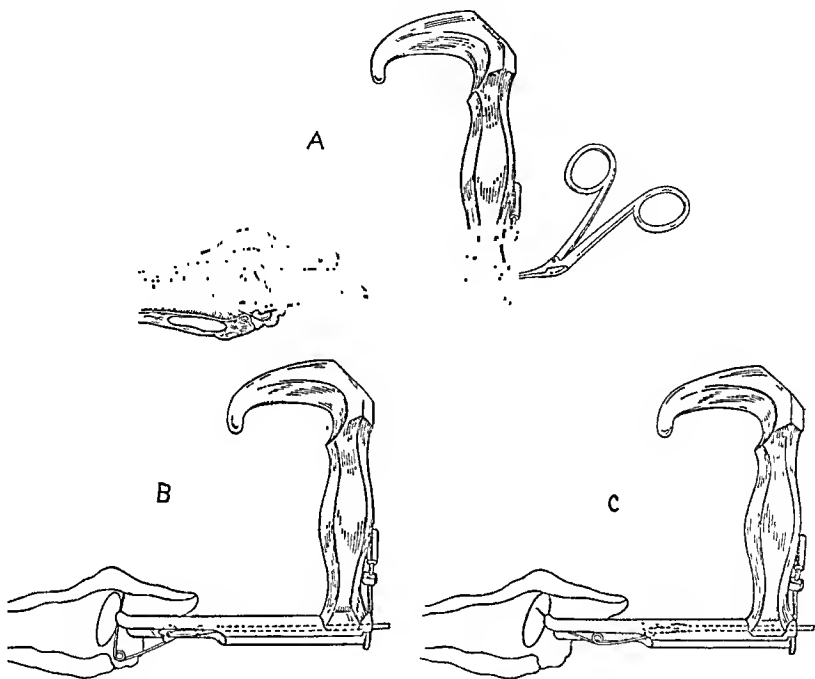


FIGURE 5 Method of Extraction from the Larynx.

A—the keeper of the pin is grasped by toggle forceps, while the tip of the laryngoscope protects the point; B—traction on the keeper is made while the laryngoscope prevents advance of the point; C—the straightened pin is withdrawn through the laryngoscope, with point trailing.

the point in the soft tissues. If, however, the point of the pin is engaged in the anterior glottic space below the point of approximation of the vocal folds, simple traction will be unsuccessful. Under these conditions, I have found the method of partial straightening of the pin through the larynx safe and satisfactory one. With the larynx exposed by the laryngoscope, the presenting keeper is grasped with toggle forceps, the keeper lying, already explained, in the sagittal plane (Fig. 5A). The tip of the laryngoscope is then held

principle presupposes that the point of the pin will not advance beyond the lip of the laryngoscope, so long as the latter is held rigidly in place, until the pin is straightened out. There is sufficient laxity of the interarytenoid space to permit the spring to rotate around the axis fixed by the laryngoscope. Even were the point to advance slightly beyond the lip of the laryngoscope, it is unlikely that any serious trauma would be inflicted in the region of the anterior commissure. With the point facing posteriorly, one might hesitate to execute

this maneuver, lest the party wall between the larynx and esophagus be perforated, but fortunately this accident is extremely uncommon.

*The bronchus.* In the event that an open safety pin of relatively small size with a necessarily less than ordinary spread passes through the larynx, it may come to rest in a main bronchus, oftenest just below the bifurcation of the trachea and usually with the point up. Such a pin could, of course, conceivably lodge in the

bronchoscope beyond the pin (Fig. 6A). The keeper is grasped with toggle forceps, and the bronchoscope slipped downward until the spring impinges on the more distal edge of the bronchoscope (Fig. 6B). The latter is then held firmly in place, and steady traction is made on the keeper, thus straightening the pin into the bronchoscope (Fig. 6C). The apparent risk of this procedure is greatly minimized by the fact that such bronchial pins usually lie with the point just

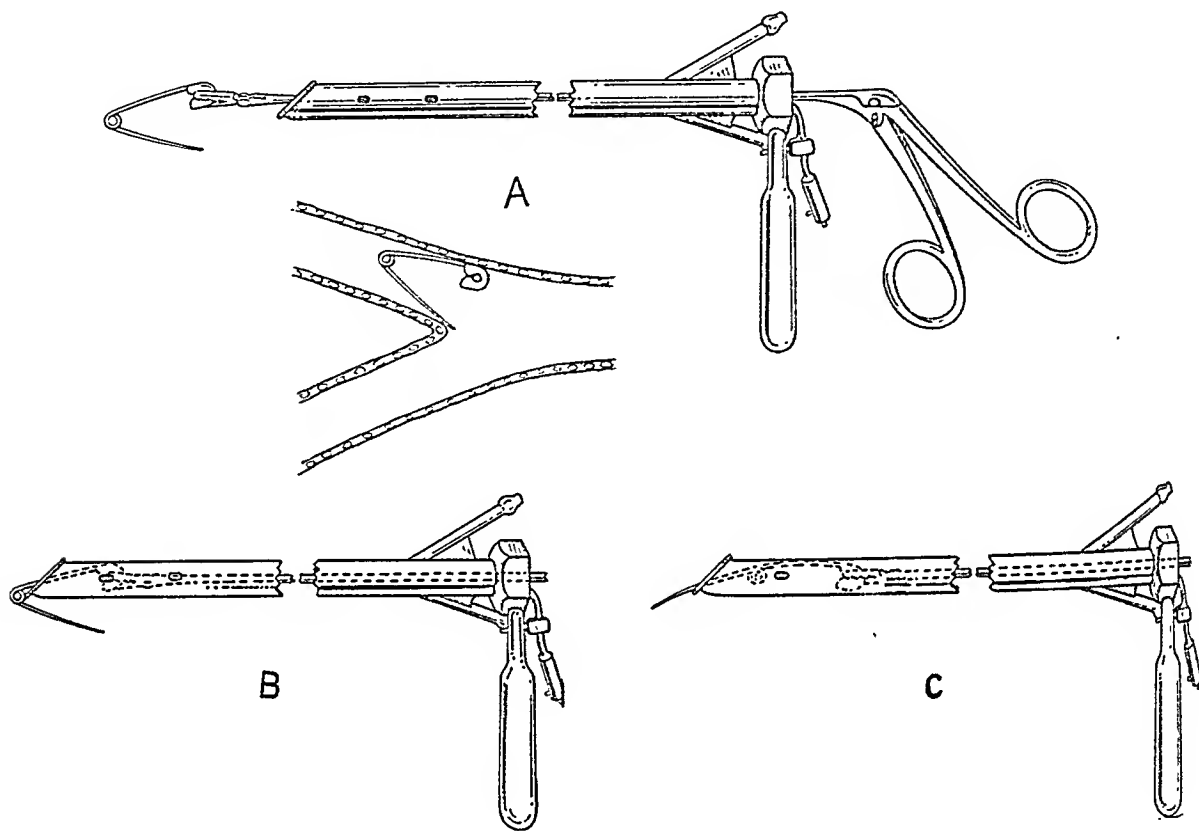


FIGURE 6. Method of Extraction from the Bronchus.

A—the pin is grasped with toggle forceps, preparatory to advance of the bronchoscope over the keeper; B—the keeper is drawn into the tube, with the lip of bronchoscope braced against the spring preparatory to straightening into the tube; C—the pin is straightened into the bronchoscope, with point trailing.

trachea, but if of sufficiently small size to pass the subglottic region, it is far likelier to descend and lodge in one or the other of the major bronchi. In my very limited experience with this situation, I have found the straightening method, somewhat as above described with reference to the larynx, to be satisfactory. It is first of all necessary to pass the bronchoscope into the invaded bronchus and visualize the keeper of the pin. The bronchoscope must be of sufficient caliber to permit, in much the same manner as the Mosher esophagoscope, the entrance of the keeper into its lumen. There is no question, however, of closure, since it is impossible, owing to the decreasing caliber of the bronchus, to advance the

proximal to the carina. As traction is made against the lip of the bronchoscope, the point tends to rotate across the carina and even into the orifice of the opposite main bronchus, thus affording it a temporary resting place until it is converted into a trailing point. As already stressed, it is of the greatest importance to know beforehand the size of the keeper and to utilize a bronchoscope the lumen of which is assuredly large enough to admit the keeper freely. In an infant, this necessity may provoke complications, since a sufficiently large bronchoscope may pass the larynx with difficulty and, later, resultant laryngeal edema may require tracheotomy. This, however, is not serious provided that the pin has been successfully

removed without trauma to the tracheobronchial tree. Fluoroscopic assistance in such a situation is not so essential as it is with pins in the esophagus, but may be of distinct assistance to the bronchoscopist.

### COMPLICATIONS

The complication most to be feared in connection with an open safety or clasp pin in the food passages is perforation of the esophagus. The wide and unyielding spread of the spring seems off hand to make this a likely occurrence in any case in which the pin is not removed immediately. Rather strangely, such preoperative perforations are quite rare, and open pins have been known to remain in the esophagus for weeks or months without perforation or serious local infection. The considerable mobility of the esophageal wall doubtless accounts for this fortunate circumstance. Hence responsibility for the definite development of alarming symptoms of perforation or mediastinal infection following attempted removal must usually be placed squarely on the shoulders of the operator, who can feel scant solace in the thought that the pin may have perforated spontaneously. Postoperative elevation of temperature, painful deglutition, a rising leukocyte count and definite roentgenographic evidence of an increasing prevertebral swelling with or without air in the tissues—any or a group of these symptoms strongly suggest the need for prompt consultation with a

thoracic surgeon, with strong probability that external drainage of the upper or lower mediastinum will be advisable. More detailed consideration of the indications for such surgery does not fall within the scope of this paper. Suffice it to say that impending tragedies have been averted by prompt resort to external drainage of an esophageal perforation.

### CONCLUSIONS

The open safety pin is a relatively common foreign body in the upper air and food passages. Early diagnosis is best assured by x-ray examination of any patient in whom such a foreign body is suspected.

Technics of removal vary with the location of the pin, but familiarity with one dependable method is more valuable than a theoretical knowledge of several. Fluoroscopic aid is indispensable in the removal of pins in the cervical and thoracic esophagus, and is a distinct aid with those in the tracheobronchial tree.

Evidence of a complicating esophageal perforation demands prompt consultation with a thoracic surgeon.

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## ENLARGEMENT OF THE HEART\*

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THERE has been a great deal of talk about congestive heart failure during the last few years—indeed, to the extent that it has taken the limelight of medical interest, so far as the heart is concerned. Important as it is, however, it is far less vital and should receive less attention by the medical profession than two other cardiac problems. The relatively greater significance of the first of these, the causes of heart damage or strain, is readily and widely admitted, but the second is often neglected and indeed sometimes forgotten, namely, heart size—whether or not there are any other abnormalities, such as symptoms, murmurs and arrhythmias.

Two hundred and sixty-two years ago, Théophile Bonet published a fundamental collection of autopsy reports, the *Sepulchretum*, which was

critically reviewed and amplified in a sort of third edition by Morgagni nearly a century later, under the title *De Sedibus et Causis Morborum*. In the original edition in 1679, there were a number of cases showing enlargement of the heart, one of these patients had suffered from shortness of breath that before death had been routinely ascribed to pulmonary disease, which was not found post mortem. The association of a serious symptom with a large heart was spoken of with surprise by the observers of that case and was evidently the beginning of the realization of the importance of cardiac enlargement. A few decades later, in 1728, there was published a book, in large part on this subject, written by Lancisi, physician to Pope Clement XI, it was entitled *De Motu Cordis* [following the post Harvey tradition] *et Aneurysmatibus*, which meant large hearts as well as large aortas.

Thus, quite rightly, the first cardiac abnormality

\*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1941.  
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of consequence to be described and studied in pathology and clinical medicine was enlargement of the heart. With the advent of auscultation, however, medical interest was turned away from heart size, on which percussion, already introduced, was unable to focus attention, and concentrated for a century or more on heart murmurs, which were too often interpreted as evidence of valvular disease. The textbooks for many decades were filled with chapters on every possible valve defect, only a few persons, like Mackenzie, trying to redirect attention to other cardiac findings, after the turn of the century. At last, cardiologists are approaching a saner and wiser viewpoint, although I dare say they are still simply in the middle of the process of proper cardiac orientation. It is this revolution and evolution in cardiovascular knowledge that has rendered a cardiologic vocation absorbing and satisfying for those who were so fortunate as to enter that field two or three decades ago.

The first of the problems of heart size is the most difficult of all, namely, the range of the normal size. It has been left to the last to study, for, fundamental though it is, it has not appealed to the pioneers who have been unearthing, with almost every spadeful, nuggets of interesting, spectacular and unusual pathologic conditions of the heart. I have been as guilty as the next man in this respect, witness to which is the record that my laboratory still holds in medical literature of enormous heart volume—seven times the normal. Now at last, except for a few who have patiently tilled the field for some years, cardiologists are turning to the more vital problem of the determination of the beginning of cardiac enlargement in any given case.

What is the normal heart size, and how can it be ascertained in a particular person? Even the anatomist, pathologist and anthropologist cannot limit the heart weight and volume for the normal person within a narrow range. Roughly, the weight of the heart has been considered normally to average 0.5 per cent of the body weight, but this is a very imperfect estimate indeed. Body build and other hereditary manifestations that have not yet been worked out are undoubtedly important correlative factors; the aid of anthropologic data is needed to secure greater accuracy of fundamental measurements, and this aid is only now beginning to be sought.

With this difficult enough problem to begin with, one now must face the additional difficulty of the clinical determination of heart size. Three methods are available. First and simplest and often quite accurate is the position of the cardiac

apex impulse by palpation. Sometimes this is easily determined, sometimes only with difficulty, and sometimes it is impossible. In those cases in which the maximal apex impulse is found in the fifth intercostal space within or on the left mid-clavicular line, one can be quite sure that there is no significant cardiac enlargement. In such cases, it is still essential to percuss the position of the left upper border in the third and fourth interspaces, — and this can be done in most cases with reasonable accuracy, — to determine if there is undue prominence of that part of the heart, a finding common in cases of mitral stenosis or cor pulmonale with an enlarged right ventricle but with the apex impulse not far from the normal position.

Next, a word is due about percussion. Inaccurate and disappointing as this method of examination may be in many cases, in comparison to x-ray study, it is often a useful procedure in many patients when x-ray examination is impracticable or not immediately possible. There are many such cases, and if one sits back with folded hands complaining of the inferiority of percussion to the x-ray film, one will miss valuable evidence of heart size that may be obtained only by percussion when the apex impulse is felt with difficulty, or not at all, and when x-ray examination is not available. It is necessary to acquire skill in percussion, which cannot be learned overnight. Most of those who scorn percussion do not want to bother to learn the technic or through long neglect have lost all confidence in it. Even though I fluoroscope each one of my patients in my office, I percuss the chest first and thereby control my percussion findings and keep up a certain practice that proves helpful when I encounter patients elsewhere, as at home. I can recommend this procedure.

Too much confidence about heart size, on the other hand, is often yielded to an x-ray report, — not that the x-ray picture per se is not correct, although even its accurate transcription and original interpretation need a check, for which more than once physical examination has served me well, — but deductions from measurements of the x-ray heart shadow must be made in borderline cases only with the greatest care. Here, too, there are wide limits of the normal, even for the same height and weight and age — so wide in fact that a good many competent and experienced roentgenologists do not bother even to make any measurements unless requested. Other roentgenologists furnish a long list of measurements of diameters, arcs, area and even volume; these are often interesting but far less valuable than an actual view of the x-ray film itself, or best of all, of the subject



in the flesh under the fluoroscope. There are too many imponderables for one to have confidence in a few ponderables, if overmuch is made of them. My own attitude is a compromise between these two extreme points of view. I favor those who scoff at emphasis on detailed measurements, and yet, poor as they may be, the measurements to my mind are better than none, for x-ray films may be lost or difficult to secure at any given moment for detailed study or comparison with previous records, and figures, rightly or wrongly, mean more to me than mere statements of normal heart size or of slight, moderate or great enlargement.

Just a brief word, before leaving x-ray heart study, about the best measurements to use. Combinations and correlations of the various diameters have been introduced, and the heart volume has also been roughly measured, but none of these procedures are practicable for routine use, because of various difficulties of technic or of wide scatter of the normal range. Three methods in common use are equally applicable to orthodiagraphy and to seven foot films, and are satisfactory in their routine employment, when one remembers that the heart shadow is larger by nearly 10 per cent in the seven foot film than in the orthodiagram. The commonest method, but one that should be discarded because its range of the normal is the widest, is the so called 'cardio thoracic ratio,' that is, the division of the transverse diameter of the heart by the internal transverse diameter of the thorax, here the normal range is tremendous, from 33 to 55 per cent. The other two methods, both open to objection but the best for routine use, are the correlation of the transverse diameter of the heart shadow with height, weight and age, according to the Hodges-Lyster formula, nomogram or slide rule, and the correlation of the area according to height, weight and age. There are special advocates of both and since the measurement of the transverse diameter is much simpler and quicker technically, I am at present using it with the help of a simple slide rule. It is as quick as and better than the cardio thoracic ratio, which I have recently discarded. Actually, however, for reliance one needs something better than anything as yet available.

The most awkward dilemma is an inability in many cases to detect the presence of slight cardiac enlargement, an early sign of serious heart strain and therefore an essential thing to know in any cardiac patient. The range of normal is so wide that any case may change from a small normal heart size to a large normal heart size without one's realization of the fact unless one has early careful measurements of that particular heart to begin with.

Formerly, cardiac enlargement was regarded as evidence that the heart was strong and compensating for whatever strain was present, but it has gradually become realized that a large heart is a bad sign and evidence that the myocardium is not a normal healthy muscle and that it is no longer able to resist the strain. It is an indication that more and more enlargement is likely to follow, resulting in myocardial failure of the congestive type, unless the strain can be eliminated. In fact, any cardiac enlargement is already evidence of some failure of myocardial strength, although not at first of the grade to result in congestion. Slight and moderate grades of increase in heart size may persist with little change for years, however, and are not to be viewed with immediate apprehension. Nevertheless, they are not good signs, and important trouble threatens if marked enlargement is found or if the size steadily increases under observation for a relatively short time.

Enlargement of the heart may be due to acute dilatation, to preponderant hypertrophy or to both hypertrophy and dilatation of comparable degree. The best theory of its onset is that it starts as an overstretching or dilatation of the myocardium and that work hypertrophy is in large part a reaction of the heart muscle to injury and a failure of the myocardium to return to its original size. Little by little, this stretching in many cases goes on until the heart becomes very heavy, although often with relatively little dilatation of the heart chambers, and the process accelerates to a state of clinical myocardial insufficiency from which congestive heart failure results.

There has been a return to the old time diagnosis of acute dilatation of the heart, once applied indiscriminately and often to the wrong patients, then two or three decades ago abandoned disdainfully, but now acknowledged as a correct appellation for certain cases. Four conditions are occasionally responsible for a fairly acute dilatation of the heart, two of which—namely, severe acute rheumatic myocarditis and excessive heart rate in paroxysmal tachycardia—affect both ventricles, the third, acute massive, myocardial infarction, involves the left ventricle primarily, and the fourth, massive pulmonary embolism, involves the right ventricle (the acute cor pulmonale). The acute dilatation may precipitate congestive failure and death, it may clear up almost or apparently completely on subsidence of the acute strain, or it may, as in many cases of acute rheumatic and acute coronary heart disease, leave permanent enlargement of the heart, consisting in both dilatation and secondary hypertrophy, which may in chronic rheumatic heart

disease be ascribed wrongly, in toto at least, to coincident valvular deformity.

Some hearts, especially those under the strain of systemic or pulmonary hypertension and of aortic stenosis, show at first and for years preponderant hypertrophy, dilating appreciably only at the time of final failure. Others, especially those with free aortic regurgitation, show much dilatation at an early stage and also the highest degrees of hypertrophy; the heaviest and often the most voluminous hearts belong in this group and have been labeled "cor bovinum." The record-breaking hearts in volume, however, are those with mitral valve disease and auricular fibrillation in which the left auricle and often the right ventricle and right auricle become enormous, whereas the left ventricle is normal or actually small.

In most cases of cardiac enlargement, the strain is left-sided, from systemic hypertension, aortic valve disease or myocardial infarction, and the left ventricle consequently enlarges first and sometimes is the only heart chamber to do so. But very frequently it becomes incompetent, and then, in order, first the left auricle, next the right ventricle and finally the right auricle become enlarged. It is enlargement of the left ventricle that increases the heart weight preponderantly; that of the left auricle displaces the greatest space.

The right ventricle is far oftener enlarged than cardiologists formerly realized, chiefly because attention has been distracted by the much more obvious enlargement of the left ventricle, and because the right ventricle has been neglected, even by the pathologist. Another reason is that when it is enlarged alone, with little or no dilatation, it may escape notice clinically even on the most careful x-ray examination, as happened in a case of extensive pulmonary emphysema recently considered at a clinicopathological conference at the Massachusetts General Hospital, in which at autopsy the right ventricular wall measured 7 mm. in thickness (normal, 3 to 4 mm.); it is quite probable, however, that an electrocardiogram would have afforded the only clue, but an essential one, in the form of a considerable degree of right-axis deviation. Finally, it should be remembered that the commonest cause

of enlargement of the right ventricle is failure of the left.

Many different factors may cause cardiac enlargement, some extracardiac, like anemia and myxedema, and some intracardiac, like rheumatic myocarditis, myocardial infarction and valvular disease. In either event, the strain may be largely acute and temporary, and the enlargement may subside; but also in either event, the strain may persist and the enlargement may become permanent. Chronic enlargement is, of course, most commonly due to intracardiac disease and systemic hypertension. Quite often, particularly in older patients, more than one factor may be active at the same time. One condition, chronic pericarditis, was once wrongly blamed as a cause of great cardiac enlargement; a pericardial effusion can of course simulate a large heart, but it really acts like occasional chronic pericarditis to constrict the heart and so to make it smaller.

The prognosis of cardiac enlargement is quickly and fairly well summarized in the observation that "the larger the heart, the worse the future." Although there are exceptions, this rule holds if other things are equal.

Finally, the treatment of cardiac enlargement is twofold: first, relief of the underlying strain, which is not always possible directly, but which one can often help a great deal by reducing other strains of daily life; and secondly, the optional routine use of a daily ration of digitalis to help to prevent or retard further cardiac enlargement and failure. It seems reasonable to give 1 or 1½ gr. of digitalis daily for this purpose; the value of this drug has not yet been proved, and it will be difficult to prove.

\* \* \*

Cardiac enlargement should be suspected in patients whose hearts are under strain, even though they are free of symptoms; it is possible to do more good at an early stage than after heart failure has set in. On the other hand, it is equally important not to establish cardiac neuroses thereby, and especially not to mistake for cardiac enlargement a heart size that is on the borderline of normal unless undue heart strain is or has been present.

## NUTRITION IN WAR\*

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DURING recent years, this nation has unquestionably been living on a dietary borderline in ability to supply the nutritional factors necessary for physiologic health. Deficiency disease is endemic in this best-fed nation because more than 40 per cent of the families do not have the money to buy food for an adequate diet, because those who have the money do not have the knowledge, interest or diet habits to buy the proper foods, and because foods have been refined, processed and canned without regard to the effects on nutritional factors. As times goes on, it is being demonstrated experimentally, clinically and in the daily life of the people that the majority are knowingly or unknowingly ailing from the insidious effects of deficiency disease.

Perhaps the most important cause of these deficiencies is a too-strict adherence to the precept "Cleanliness is next to Godliness," for Americans have insisted that their foods be whitened, polished and refined. In removing the color from foods, they have unconsciously destroyed the precious compounds on which, as an evolving race, they developed a dependence.

Eight decades ago, the roller-mill process for flour manufacture was invented, and today all white flour is made by that process. Jolliffe<sup>1</sup> has calculated that, to obtain the thiamin lost by consuming this white flour instead of the stone-milled flour of one hundred years ago, one would have to consume each day, in addition to the ordinary diet, about 1½ pounds of fruit, 1½ pounds of potatoes, 2 pounds of other vegetables and 1½ quarts of milk. Because it is difficult to increase one's food intake by so large an amount, and because such a procedure would be expensive, population groups with low incomes have suffered most from the refinement of the dietary and show the highest incidence of deficiency disease. The poor are of prime importance in considering measures to eliminate this condition, for those in higher economic brackets can more or less successfully, but not with certainty, make up for the losses caused by refinement by consuming more fresh vegetables and fruit.

The amount of bread consumed by a community

is usually in direct proportion to its economic status, for bread is the food of the poor. It was fundamentally sound, therefore, when the Committee on Food and Nutrition of the National Research Council was organized last fall, that its first action<sup>2</sup> was to decide the vitamin and mineral potencies that bread and flour should have to make these staple foods, which together constitute one fourth of the average calorie intake, carry their rightful nutritional quotas. Bread will become a staff of life on which man can again lean for true nourishment.

It is expected that cereal food products will be similarly enriched, and that the slight cost will be absorbed by the manufacturers. It is hoped, also, that the Committee on Food and Nutrition will continue to catalyze improvements in the basic foods of the poor, especially sugar and fats, and to encourage the consumer to purchase those inexpensive foods that will give him the most for his food dollar.

The problem confronting this committee is to see to it that the foods most readily available, the staple foods, are so nutritious and still so inexpensive that it would be exceedingly difficult for a person with little knowledge of nutrition to select a diet that would be deficient over a reasonable period.

Why is this especially significant at this time? Because an ill-fed nation is a sick nation.

Drummond and his group,<sup>3</sup> for example, made a comparative study of the life history of two groups of rats, one of which (483 animals) was maintained on what they called an "adequate" diet and the other (556 animals) was fed a diet providing a suboptimal intake of the vitamin B complex, the chief defect being that of vitamin B<sub>1</sub>. The life span was shortened, reproduction was impaired, and the incidence of gastrointestinal lesions was definitely increased (Table 1).

In similar experiments, McCarrison<sup>4</sup> apparently used a more adequate diet than Drummond, for he noted no gastrointestinal disorders in rats, rabbits, dogs and monkeys fed on this diet, whereas animals on a diet deficient in minerals, vitamins and proteins, and identical to the dietaries of a large mass of people, showed some gastrointestinal or organic disorder, usually several. Numerous other experimental and clinical results clearly indicate the great value of good nutrition and lead one to ask whether many of the maladies of to-

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day are the result of malnutrition and under-nutrition.

At the beginning of this century, it was thought that nutrition consisted in supplying calories for fuel, protein for muscle formation, water and a

TABLE 1. *Effect of Subsistence on Diet Deficient in Vitamin B Complex.*<sup>3</sup>

GASTROINTESTINAL LESIONS	ADEQUATE DIET (483 ANIMALS)	INADEQUATE DIET (556 ANIMALS)
Dilated stomach	9	60
Gastric erosion	27	88
Chronic gastric ulcer	27	80
Perforated ulcer	1	7
Hair balls	8	44
Distended intestine	22	52
Intestinal ulcer	4	17
Cecal ulcer	8	42
Perforated ulcer	2	4

few minerals, such as calcium, phosphorus, iron and iodine. Foods were analyzed on that basis, and diets were formulated in terms of calories.

TABLE 2. *Nutritionally Essential Factors.*

CALORIES (carbohydrate and fat)			
PROTEINS (aminoacids)			
Phenylalanine	Methionine	Histidine	Leucine
Tryptophane	Isoleucine	Arginine	Lysine
Threonine			Valine
VITAMINS			
Vitamin A		Pyridoxine	Vitamin D
Thiamin (vitamin B <sub>1</sub> )		(vitamin B <sub>6</sub> )	Tocopherol
Riboflavin		Biotin (vitamin H)*	(vitamin E)
(vitamin B <sub>2</sub> )		Para-amino benzoic acid*	Vitamin K
Nicotinic acid		Ascorbic acid	Choline
Inositol*		(vitamin C)	Linoleic acid
Pantothenic acid			
MINERAL ELEMENTS			
Calcium	Sodium	Chlorine	Zinc
Phosphorus	Potassium	Sulfur	Iodine
Iron	Magnesium	Copper	Cobalt
	Manganese		
WATER			

\*Evidence of human needs is fragmentary.

It is now realized that nutrition is much more involved, and that more than three dozen substances and elements are required for normal physiologic functioning (Table 2). Each of these substances must be supplied in adequate amounts else deficiency disorders will result.

Nutrition of Armed Forces

Since the majority of the American people have minor nutritional ailments and a very substantial minority are definitely deficient in several nutritional factors, a good proportion of the men entering military service are undernourished. They are being given nutritionally balanced diets definitely superior to those on which they lived at home. One can therefore expect an improvement in the health, vigor and mental and physical stamina of these men. Military authorities are keenly aware of the importance of sound nutrition in preserving

the morale of the men, and they are constantly being advised by the best medical and nutritional experts in an effort to make the American soldier and sailor the best fed in the world.

The value of good nutrition to a nation at war is shown in the recent reports by Williams and his co-workers,<sup>5, 6</sup> who found, for example, that, in an experimental group, a diet deficient in thiamin produced moodiness, sluggishness, indifference, fear, depressed mental states, mental fatigue, dizziness, backache, insomnia, anorexia and physical fatigue. Morale and stamina cannot be expected of thiamin-hungry troops or populations.

The German high command has long studied the problem and has made painstaking preparations lest the present war be finally lost owing to the malnutrition of the German troops and peo-

TABLE 3. *Cost of Important Vitamins Required by an Adult.*

VITAMIN	DAILY OPTIMUM	COST PER DAY
A	5000 int. units	\$0.0003
B <sub>1</sub> (thiamin)	2 mg.	0.0013
B <sub>2</sub> (riboflavin)	3 mg.	0.0030
Nicotinic acid	20 mg.	0.0003
C (ascorbic acid)	75 mg.	0.0053
D	400 int. units	0.0001
		\$0.0113

ple. In World War I, malnutrition was a powerful factor in leading the Central Powers to seek an armistice. The food blockade of that war was so effective that starvation and its accompanying deficiency diseases were rampant in the general population. The advances that have been made in nutritional science since 1918 have been so great as to make it almost impossible to blockade the Nazi nation. All the important vitamins man needs can now be synthesized within Germany at little cost.

Today, the American manufacturer of food or vitamin products can purchase these vitamins for so little that a daily optimum costs less than 12 cents (Table 3). If the Government were to supply a population of 50,000,000 with these needed vitamins, the basic cost would be only \$206,000,000 yearly. Since these current prices in America are undoubtedly higher than those in Germany, it is evident that the Nazi command can easily supply sufficient vitamin supplements to protect the German armies and people against vitamin-deficiency disease, especially since a goodly fraction of the vitamin requirements can be contributed by rationed foods and ersatz.

Although vitamin starvation had much to do with the defeat of the Central Powers during World War I and would likely not be a factor in the defeat of the Axis in the present conflict,

protein starvation may be a significant factor. Calories can be obtained from many kinds of foods, vitamins can be synthesized in the chemical laboratories, minerals can if necessary be provided in the form of inexpensive tablets, but the protein requirements of a people cannot be met without good foods. The constituent aminoacids of proteins are needed for the formation and replacement of muscle tissue, and the special functions of many of these aminoacids cannot be performed by any other compound; only a few of these acids can be synthesized cheaply by the chemist.

A nation at war must have adequate supplies of good proteins if it is to survive. Therefore, foods rich in excellent protein (meat, milk powder and cheese) are today preferred for shipment to England.

The proteins of plant tissues are generally inferior to those of animal tissues because they are deficient in one or several of the essential aminoacids. It is, of course, possible to combine plant proteins in the dietary or in food mixtures so as to obtain adequate amounts of these aminoacids, but this requires special knowledge.

It has been authentically reported that the German forces, in garrisons and in active warfare, are living on dried foods and dried food mixtures. During the last ten years, the German government has fostered considerable research and developed methods for dehydrating foods without destroying nutritional factors and changing the taste. Without doubt, Germany stands far in advance of other nations in this vital field of food technology, which has not had the proper development in this country. The Nazi armies can be fed with tasty, nutritious, dehydrated foods, which require no refrigeration and are one fifth as bulky as ordinary foods. The rapid maneuvers and advances of the *Panzer* divisions in recent battles would have been difficult without this simple method of feeding.

Furthermore, in these rations, plant proteins rather than animal proteins have been used. It would be difficult to supply animal proteins during a long war, for the fodder needed by the livestock cannot be imported. For many years there has been an intensive planting of soybeans in the Balkans, in Bessarabia and in Germany. This interesting legume, long a staple food in the Orient, will grow on a variety of soils, requires little attention, and yields a food protein the important aminoacids of which approximate, in variety and proportion, the proteins of meat, milk and egg. Although considerable reliance is being placed on soybean protein, it is not certain that enough is being produced to meet Axis needs.

But this would be of no consequence, since one can be sure that the Nazi command will allow protein starvation to appear in the conquered nations and use their foodstuffs in feeding the Nazi armies and the German population.

Although it is my belief that the Axis will not be starved out of this war, there is a grave possibility that England will be counterblockaded into starvation: protein starvation, vitamin starvation and, eventually, calorie starvation. Britain has long been an industrial nation, importing raw materials and exporting manufactured goods, meanwhile relying on importations to supply 40 per cent of her food. She has lost several neighboring islands from which important quantities of vegetables and dairy products have been received in the past. She could not import enough fodder for her pigs, poultry, sheep and beef cattle, and has slaughtered many.

However, Britain has increased the number of milk cows so that an unrestricted amount of milk will be available to nursing and expectant mothers, to young children and to hospitals. Over 2,000,000 acres of grassland have been plowed up in response to a bonus of £2 per acre and planted mostly with grains (barley, oats and wheat). British leaders have stressed the point that malnutrition can be avoided with sufficient milk, vegetables and potatoes, and that starvation can be prevented with sufficient bread, vitaminized fat, potatoes and oatmeal. Imports of fats, sugar, dried fruits, frozen meats, canned meats, canned tomatoes, milk powder and cheese have been preferred, for these foods have high-calorie content per ton of shipping space, contain fine proteins and critical vitamins, and supply the special needs of the British people.

Foods such as meat, fats, butter and sugar have been rationed along with many nonessential food items. Any war involves a marked simplification of the foods of the people, with an accompanying loss in palatability and richness and a limitation of choice. There is evidence of reduction in body weight in some sections of the population. So long as this restriction is not great, the rationed peoples may be well off, since they report that they feel better. Severe restriction would be serious since, even in normal times, one must consume more than 1900 calories as food daily to obtain needed vitamins. The best choice of foods supplies less than three quarters of the required daily vitamin needs, with the possible exception of ascorbic acid. Thus, adults have a choice between deficiency disease and gluttony. If one can judge from the appearance of the adult population, they are choosing gluttony—the better choice under the circumstances. Is there not some rela-

tion between the good nature of the fat man and his better nutrition?

Rationing of food is not new; in fact, it is an integral part of planned economy. It need not work hardship on a people or adversely affect its morale. The poor have always been rationed, for poverty limits their choice of foods. Furthermore, since the people of a warring country are now truly in the front lines, they must be ready to resign themselves to the restrictions and methods of the soldier, even to the extent of eating concentrated food mixtures.

It should be pointed out that concentrated mixtures consist of several foods, cooked separately, blended and mixed; they are not ersatz in any sense, since only water is removed. That is all that can be done, because one cannot concentrate the 3000 calories or the 100 grams of protein that an adult needs daily. Test-tube feeding or capsule feeding is the invention of the newswriter, for adult man cannot be fed on less than  $1\frac{1}{3}$  pounds of concentrated foods daily.

### *Feeding the Population in War*

Research has shown that visual acuity, mental and physical health, morale and endurance may be impaired by nutritional deficiency. It is therefore imperative that workers connected with defense industries be well fed. It may be advisable to imitate England's soup kitchens by feeding the workers in these vital industries nutritious mid-day meals. Field tests have shown that the improvement of substandard diets in groups of workers results in increased output and a reduction in accidents.

One of the most important functions of the Government is the school-lunch program, which endeavors to feed needy children with surplus foods. In the present war, this program should be extended to include all undernourished children and to improve the lunches so that an adequate diet will be assured. The effect of a continued program on the health of these children and on their future usefulness to themselves and

others cannot be predicted too optimistically. Clinical experiments have shown its advantages.

Some method will have to be devised to care for the remainder of the population who cannot afford an adequate diet. Until then, the admirable Food Stamp Plan should be extended. Certain foods now purchased under this plan may soon lose their status. In fact, it appears that wheat is the only true surplus, and efforts should be made to curtail its production. Soybean, peanuts and similar foods of superior nutritive value should be grown in its stead.

### *Postwar Problems*

When the present conflict is over, there will be millions in various degrees of starvation who will need to be fed. There are millions today in this condition, but they cannot be reached. One can only hope that they will survive to the armistice. Hundreds of thousands will undoubtedly perish, the victims of disease resulting from their nutritional deficiencies. Those who survive may long carry the scars of their starvation, possibly into future generations. In looking ahead to the day when these unfortunate people may be fed, groups are anticipating the needs and devising a program to fill them.

\* \* \*

This is a critical and unhappy era. We can properly feed our own people and assist in the feeding of our valiant democratic allies. Britain must not be starved into submission. When the war ends, it will be our duty to help in the feeding of unfortunate peoples made destitute by war. This is the challenge on the food front—and we must meet it.

Charles River Road

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## MEDICAL PROGRESS

## ARTERITIS: DISEASES ASSOCIATED WITH INFLAMMATORY LESIONS OF THE PERIPHERAL ARTERIES\*

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BY usage, the term "arteritis" refers to inflammatory conditions of the arterial vessels other than the aorta. Although in recent years significant advances have been made in the knowledge of arterial diseases characterized by inflammatory reactions within and without the vessel walls, this group of disorders still represents a difficult and confusing problem to many physicians. This report discusses only the more important conditions.

To understand the arteritides, consideration of the following facts is essential:

The arteries, like other organs, respond to many pathogenic agents, but with limited types of physiologic and tissue reactions. Several noxious agents of varied character often produce identical types of physiologic and morphologic vascular changes. For example, the same type of acute arteritis can be induced by infections, transplanted homologous adrenal glands, vaso-spastic drugs and exposure to cold. Hence, from a given type of histologic reaction alone, conclusions about the specificity of the pathogenic factors cannot necessarily be drawn.

The same type of arteritis can be associated with more than one clinical picture. Therefore, the morphologic knowledge of these diseases should not be confused with the clinical aspects of the problem. It is only recently that the clinical features have been adequately studied. In the past, interest has been mainly morphologic.

Acute arteritis is not always of infectious origin, because, as in other tissues, infection is but one of the causes of inflammation. Thus, persistent spasm, like that induced by ergot, causes an acute arteritis that is identical in morphologic composition to that caused by certain virus diseases.

During the healing stage, acute arteritis usually changes into fibrous and degenerative lesions. Again, the characteristics of the healing process

are usually the same in a number of diseases affecting the arteries. Arteriosclerosis is therefore merely the chronic tissue response to several different types of persisting noxious stimuli.

Various types of injury to the endothelial layers of the arteries are apt to be followed by thrombosis. Thromboangiitis obliterans is accordingly the result of several types of arterial disease.

Although cellular reactions in the myocardium, — called "Aschoff's bodies," — verrucous endocarditis and thickening of the cardiac valves and of the chordae tendineae occur particularly often in rheumatic fever, these cardiac lesions are not absolutely specific of this disease alone. They occur also in certain other conditions associated with affection of the arteries, skin, serous membranes and joints.

## PERIARTERITIS NODOSA

Arteritis associated with perivascular reactions occurs under many conditions. Thus, disseminated lupus erythematosus, dermatomyositis, typhus fever, rheumatic fever, multiple sclerosis and chronic pyelonephritis can be associated at times with localized arterial lesions like those of periarteritis nodosa. Periarteritis nodosa, however, in a *clinical sense*, as originally described by Kussmaul and Maier,<sup>1</sup> refers to a chronic systemic disease of obscure origin and, usually, with a serious prognosis. At present, about 350 to 400 cases of periarteritis nodosa have been reported in the literature. In only 50 or 60 cases, however, has the diagnosis been made clinically. Now that the clinical aspects of the disease are becoming crystallized, this number may be expected to increase rapidly.

From an analysis of the literature, the following general facts emerge. The disease is probably not so rare as observers have thought, and is three to four times commoner in the male than in the female. It can occur at any age, cases having been reported as early as three months and as late as seventy-eight years.<sup>2</sup> It usually occurs between the ages of ten and forty. The disease is not invariably fatal, and it is probable that the prog-

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nosis will improve, when the disease is oftener recognized clinically. The clinical picture varies strikingly, depending on the distribution, severity and persistence of the vascular lesions. Practically any organ can be affected and can be the source of symptoms or signs. It is consequently essential that in patients with bizarre and obscure symptoms suggesting infectious, rheumatic or cachectic disease the possibility of periarteritis nodosa always be considered. The onset is usually gradual. Remissions, long intermissions and exacerbations are common. If fever, cutaneous or subcutaneous nodules, aneurysms of either the large or small arteries, neuritis, asthma, cardiac and abdominal symptoms, pain in muscles and joints, and eosinophilia are present, the clinical diagnosis is more suggestive, but it must be realized that these so-called "characteristic features" are often absent entirely or for a long time. The nervous system is involved more frequently than is usually suspected. Arterial hypertension is present in only a small percentage of the cases, and this depends on an ischemic involvement of the renal arteries. The renal arteries, on the other hand, are frequently involved, although there is no hypertension. The value of recognizing the skin manifestations lies in the fact that such recognition makes diagnosis of the disease possible by biopsy. The veins, as well as the arteries, are occasionally affected.

In 1936, Spiegel<sup>3</sup> reported 17 cases and discussed the clinical aspects of the disease. She emphasized the fact that 7 of the 17 patients suffered from recognized prodromal illness of a "banal" type, such as acute tonsillitis, acute sinusitis and sensitization asthma, which then — without any intervening period of good health — merged with symptoms attributable to periarteritis nodosa. Scarlet fever of atypical form occurred in 2 other patients in the two months preceding the appearance of arteritic symptoms.

In 11 patients, abdominal pain was the first symptom attributable to the vascular lesions. Almost simultaneously, 5 suffered from arthritic pain, and 2 others had cardiac and nephritic symptoms. One suggestive diagnostic association was the combination of abdominal pain and apparently unconnected symptoms such as arthritis, nephritis and cardiac insufficiency. All the 15 cases with post-mortem studies showed cardiac involvement. Twelve had lesions of the coronary arteries of varying degree, and 4 had Aschoff bodies. One patient presented the clinical characteristics of an indeterminate type of verrucous endocarditis. Periarteritis nodosa of the pulmonary arteries was present in 5 cases, and it is of interest that in 6 there were pulmonary lesions not directly depend-

ent on arteritis. Pleural pain, asthma and typical bronchopneumonia may be clinical manifestations. In some of the patients, the roentgenologic findings suggested bronchopneumonia or small pleural effusions. It is of interest that in Spiegel's series 7 patients had surgical complications because of vascular lesions of the gastrointestinal tract. Hemorrhagic pancreatitis occurred in 3 cases. As many as 8 patients had neurologic symptoms; in 6, there was a clinical impression of encephal meningitis. The lesions indicated productive perivascular and meningeal reactions.

One or more of the following lesions occurred in 12 patients: erythematous macular papules, purpura, urticaria, herpes, edema, pulsatile nodules and white-centered petechiae. Retinal exudates, neuroretinitis and thinning of the retinal arteries occurred in association with renal involvement. One patient showed a characteristic nodule of the choroid on microscopic examination. Twelve patients had polyserositis. The leukocyte count reached 54,000 in 1 patient; polymorphonuclear leukocytes were predominant, although eosinophils and monocytes were also noted.

Leishman<sup>2</sup> has analyzed the clinical features of the cases reported in the literature. The symptoms and signs in order of frequency are as follows: fever (100 to 101°F.), weakness, albuminuria, cylindruria (hyaline and granular), leukocytosis, anemia, tachycardia (out of proportion to the fever), abdominal symptoms, polyneuritis, polyserositis, edema, cutaneous lesions, cardiac signs, enlargement and tenderness of the liver but not the spleen, respiratory symptoms and albuminuric retinitis.

More recently, Grant<sup>4</sup> has made an excellent study of periarteritis nodosa. He points out that the condition is less acute and less frequently fatal than is generally thought. Thus, of 7 patients in whom the disease was clinically diagnosed in 1937, only 3 died in 1940. He studied the characteristics of the vascular lesions and described them as a necrotizing arteritis or a hyaline or fibrinoid necrosis of the arterial wall, with surrounding inflammatory reactions. The necrosis affects mainly the inner part of the media and the subintimal regions, although the whole thickness of the wall may be involved. Either a segment of the arterial wall or its entire circumference may be affected, but commonly only short stretches of the vessels are attacked. The points where the smaller arteries branch off are particularly susceptible. The portions of the artery involved become disorganized, and the internal elastic lamina breaks up, with the result that aneurysms may form. Hemorrhages may occur within the arterial walls or in the sur-



rounding tissues. Thrombi often form within the vessels. The adventitia and surrounding tissues may be swollen or may, on the other hand, show little change. The type and degree of cellular reaction varies considerably, depending on the cause and the stage of the disease. In some cases, the histologic picture is almost that of purulent inflammation; in others, there is but a slight reaction. Usually, the reaction is subacute and contains polymorphonuclear and mononuclear cells, lymphocytes and plasma cells. Giant cells are present in some cases, and eosinophils may occur. In some cases, the arterial lesions may heal, forming granulation and scar tissue, with the result that the wall becomes thickened and the lumen narrowed. No features distinguish this healing process from other types of healing or healed arteritis.

The lesions often develop in crops. Usually, the small arteries and arterioles are affected. The larger arteries become involved indirectly through their nutrient arteries. It is relatively rare for the lesions to be visible to the naked eye. Because often only a small stretch of the artery is involved, it is advisable to examine the excised tissues in serial section, not to miss the affected vascular areas. Rarely, the veins are also affected. The arteries of the heart, kidneys, gastrointestinal canal, pancreas, liver, spleen, skeletal muscles, skin and central nervous tissue are usually the seat of the disease. The facts that necrotic foci of the skin and the myocardium can occur without vascular lesions and that vegetations may rarely develop over the endocardium indicate that tissue lesions can develop independently of vascular lesions. Degeneration, infarcts, necrosis, fibroses and hemorrhages may occur in various organs, depending on the location and specific characteristics of the vascular lesions. Ulcerative lesions of the gastrointestinal canal, nephritis, nephrosclerosis, fibrosis of the liver, nerve degeneration and cutaneous lesions may develop.

According to Grant's experience, the clinical onset of the disease is gradual. Malaise and rheumatic pains, with or without fever, may be the only symptomatic manifestations for a long time. Fever may be absent, low or septic. There may be considerable weakness and wasting. Skin lesions, if present, show much variation: simple erythema, erythema multiforme or nodosum, subcutaneous nodules, and pustular or necrotic lesions. Respiratory manifestations such as bronchitis, asthma, bronchopneumonia, pleurisy and infarcts are relatively often present. Tachycardia, congestive failure, nonbacterial endocarditis, pericarditis and angina are the usual cardiac signs. An unexplained and rather rapidly progressing hypertension has indicated the diagnosis in a few cases. In

about 80 per cent of the cases, albumin, hyaline and granular casts, a few red cells, gross hematuria and renal failure occur in various combinations. On rare occasions, Raynaud's syndrome, with or without subsequent gangrene, may occur. Digestive symptoms, such as vague abdominal discomfort, pain, constipation and diarrhea, are frequently present. At times, a so-called "acute abdomen" indicates surgical intervention. There may be blood or mucus in the stools. The ulnar, radial and anterior tibial nerves are particularly affected by the disease.

Ketron and Bernstein<sup>5</sup> studied the cutaneous manifestations of periarthritis nodosa. In their experience, the skin was affected in only about 25 per cent of the cases. The nodules appeared within the skin or subcutaneously, were usually not painful, and could disappear within several days. Erythemas, including scarlatiniform rashes, purpura and vesicular lesions were also present. If the larger cutaneous arteries were involved, the vascular lesion was usually typical, but lesions of the smaller arteries were often not characteristic.

The interrelation between asthma and periarthritis nodosa has been investigated in a selected group of cases by Rackemann and Green.<sup>6</sup> Of the 8 cases reported by them, all were women but 1. This is of interest because in the unselected groups the males predominate. Six patients developed asthma before the age of thirty-six years, and in most the course was short. In all the cases, the asthma was intrinsic in type. Four of the 8 patients had had trouble with the nose and sinuses. It is of particular interest that each of the 8 cases with asthma had an intense type of eosinophilia, in 3 reaching as high as 70 per cent of the white blood cells. The total white-cell count was also elevated, sometimes to 25,000 and in 1 case to 50,000. It should be pointed out, however, that this group was selected according to the observers' special interest in asthma. A study of the literature indicates that asthma does occur, but only in 10 per cent of the cases, and even when present is not always associated with eosinophilia.

Kernohan and Woltman<sup>7</sup> have studied the nervous system in 5 cases with periarthritis nodosa. In 3 cases, the peripheral nervous system was widely degenerated; in 1, the brain, and in 1, the choroid of the eye was involved. In only 1 case were the nutrient arteries to the peripheral nerves affected in the inflammatory process. The degeneration of the peripheral nerves appeared to be the result of occlusion or marked narrowing of the lumina of the nutrient arteries to the nerves. The degeneration, which was diffuse at lower levels, began as infarction at higher levels. No inflammation of the nerves was observed.

More recently, involvement of the central nervous system in periarteritis nodosa has been discussed in the German literature, but some of these publications have not been available. Stanojevic and Dimitrijevic<sup>8</sup> reported a case with involvement of the central as well as the peripheral nervous system. There were also changes in the eyegrounds designated as "neuroretinitis angiospastica," with early manifestations of retinal detachment. Since the patient also had hypertension, it is questionable whether these eyeground changes were specific. Judging from a study of the literature, I believe that these changes, if they do occur in periarteritis nodosa, usually depend on the associated hypertension. Rarely, however, as in the case reported with histologic findings by Gjertz, Nordl w and Svenmar,<sup>9</sup> the affection of the retina depended on typical lesions of the vessels. It is of interest that this patient also suffered from episcleritis.

Sawyer,<sup>10</sup> Allen<sup>11</sup> and Mondor, Ducroquet and Olivier<sup>12</sup> have reported on the surgical aspect of periarteritis nodosa. Occlusion or aneurysmal rupture of large or small arteries of various abdominal organs may lead to symptoms and signs imitating those of penetrating peptic ulcers, chronic cholecystitis, perinephritic abscess, pancreatitis, mesenteric infarction and peritonitis. Even the liver may be affected.

#### THROMBOANGIITIS OBLITERANS

Although this arteritis was described as "endarteritis obliterans" by von Winiwarter as early as 1879, and although it has been intensely studied since 1908 by Buerger and others, several significant aspects of the disease remain obscure. Not only is its etiology unknown, but the chronic stage of the disease is still confused with certain types of arteriosclerotic degeneration of arteries of the lower extremities. One needs particularly to know more of the early stage of the disease. It is surprising how few studies of biopsied specimens are available from this stage, when not only are the symptoms vague (paresthesias) but laboratory methods may even fail to demonstrate ischemia. In my experience, during the acute and the early stages, several characteristics of the disease may closely simulate those of periarteritis nodosa. At times, only the physiologic evidence of involvement of the larger arteries of the extremities may be the differential point.

In the recent literature, controversy about the etiology of thromboangiitis obliterans continues. It is probable that it can be caused by a number of factors, and frequently several of these factors seem to act synergistically. Recently, Good-

man<sup>13</sup> brought forward further evidence in favor of the rickettsial origin of the disease in at least one group. He claimed that thromboangiitis obliterans is a late manifestation of typhus fever. Gangrene as a direct complication of typhus fever has been reported repeatedly in the literature. Goodman also claimed that wherever typhus fever is endemic, there is a high incidence of thromboangiitis obliterans. In 100 cases of thromboangiitis obliterans studied by him, all patients gave a positive skin reaction following the intracutaneous injection of the rickettsia suspension. In 93 per cent of a corresponding number of control cases, this test was negative. In 100 cases of Brill's disease, it was 97 per cent positive. It is of interest in this connection that, in 1939, Parker<sup>14</sup> reported thromboangiitis obliterans as one of the complications of Rocky Mountain spotted fever and mentioned the frequency with which gangrene of the extremities was observed in animals inoculated with the rickettsia of this disease. Jordanus, as quoted by Goodman, described the sixteenth century epidemic of typhus that swept the Continent from Russia and caused millions of deaths. He mentioned as its chief features high fever, prostration and gangrene. Goodman also stated that in Japan "juvenile gangrene" is very common, and that rickettsial diseases, particularly tsutsugamushi, are likewise common. The vascular lesions in typhus fever, as described originally by Fraenkel,<sup>15</sup> consist of necrosis of the media of the small arteries within the cutaneous roseola, often associated with cellular reactions around the vessels. Fraenkel states that these vascular reactions remind one of those found in periarteritis nodosa, although the two diseases are not related to one another.

Arterial thrombosis of the extremities can occur, however, in a number of contagious diseases. Hoyne and Smollar<sup>16</sup> report the occurrence of gangrene of the lower extremities as a rare complication of scarlet fever. These writers were able to find in the literature 17 cases of such gangrene associated with scarlet fever. In 5 of these, the gangrene was bilateral, and in 16 it was so-called "dry gangrene." In 1 case reported by Hoyne and Smollar, there was an acute myositis above the area of gangrene, associated with panarteritis of most of the arterioles. In another, reported by Hoyne in 1915, dry gangrene of all four extremities developed, and in addition both ears and both cheeks were affected. It has been estimated that gangrene of the extremities occurs only once or twice in 30,000 cases of scarlet fever. This complication does not depend on the severity of the illness, but is considered as an unusual arterial response of the host.

In recent years, an increasing number of cases of thromboangiitis obliterans with central-nervous-system manifestations have been reported. These nervous symptoms may appear during either the acute or the chronic (arteriosclerotic) stage. Lindenberg<sup>17</sup> reports the affection of the central nervous system in this disease. He states that thromboangiitis obliterans is primarily a morphologic condition due to several agents. The effect on the central nervous system manifests itself in granular atrophy, with multiple small softened areas. In some cases, the distal small branches of the larger cerebral arteries are affected, whereas in others the vascular affection shows completely irregular involvement. Histologically, the lesions represent an endarteritis with thrombi. The media is relatively free. A perivascular inflammatory reaction may also be present. In chronic cases, the intima of the involved arteries is thickened. Recanalization of thrombosed arteries occurs frequently. The clinical manifestations are varied. Transient headaches, palsies, syncope and convulsions are prone to occur. The disease may imitate Alzheimer's disease.

The interrelation between thromboangiitis obliterans and the retinal vessels is of some interest. This topic has been discussed and reviewed recently by Wagener.<sup>18</sup> According to Wagener's report, Marchesani was impressed by the association, in a group of young persons, of recurrent hemorrhages into the retina and vitreous on the one hand, and transitory severe cyanosis of the extremities and trophic disturbances in the nails and skin on the other. In a number of these patients, there were no pulsations in one or more of the arteries of the lower extremities. All showed dilatation of the venous loops of the capillaries of the nailfolds, often associated with capillary hemorrhages. In the series of 22 patients reported by Marchesani, 2 suffered from gangrene of the toes, and 1 from gangrene of the fingers; 19 had evidence of "latent" Buerger's disease. In 1 case with gangrene, histologic examination revealed variable narrowing of the lumens of the smallest retinal vessels, which was due to swelling of the subendothelial tissues. In some of the larger arteries and veins, the endothelial layers were destroyed and the lumens filled with fibrinlike material. Other lumens contained material rich in cells. It is interesting that vessels of the iris and of the ciliary body were also involved. Marchesani suggested that these lesions of the vessels of the eyes were the ocular manifestations of Buerger's disease. Three of Marchesani's patients with primary symptoms of retinal periphlebitis showed atypical multiple sclerosis. Wagener states

that in the Mayo Clinic in a large series of patients with Buerger's disease he had but few cases of thrombosis of the retinal vessels. In 1 patient with presenting features of recurrent hemorrhages into the vitreous, typical manifestations of Buerger's disease developed years later. Other reports in the literature on the interrelation of eye symptoms associated with recurrent hemorrhages in the vitreous or vascular lesions in the retina on the one hand, and vascular affection of the extremities on the other, are summarized by Wagener. It is questionable whether in all these cases the ocular disturbances are manifestations of thromboangiitis obliterans, as originally suggested by Marchesani.

Since the chronic manifestations of thromboangiitis obliterans are adequately recognized, and since no outstanding contribution has been made recently to the knowledge of this phase of the disease, discussion of it will be omitted.

#### TEMPORAL ARTERITIS

Since the first case of temporal arteritis, reported in 1931, further cases of a similar nature continue to appear in the literature. Recently, Sprague and MacKenzie<sup>19</sup> have reported the case of a sixty-six-year-old man who complained of temporal neuralgia after a vague onset, and subsequently of temporomandibular arthralgia. The fact that in this patient, as has been true in other cases, the localized arteritis was associated with generalized debilitating conditions indicates that arteritis is a manifestation of a generalized disease. Bowers<sup>20</sup> summarizes the histologic findings in temporal arteritis. That the medial coat is usually affected is indicated by the presence of necrosis, at times with hemorrhage. The destroyed areas are replaced by granulated tissue in which giant cells are present. If all the coats are involved, there is intimal thickening and round-cell infiltration of the adventitia. The process may extend to tissues around the arteries. The lumens of the vessels may become closed. Both sexes are affected, and the patients are usually elderly, with signs of hypertension and arteriosclerosis. The cause of the disease is unknown, and its duration may range from five to six months, with some tendency to relapse, but with eventual complete recovery—in my experience, the duration has at times been but a few weeks. The cerebral, retinal and radial arteries can also be involved. In the case reported by Bowers, the occipital arteries were also affected.

Symptoms such as dull throbbing headaches, which become worse at night, fever, night sweats, poor appetite, loss of weight, anemia, weakness and mild leukocytosis may precede by several weeks

local signs of inflammation of the arteries. Small nodules may be felt over either the main branches or the smaller ones.

Recently, Hoyt, Perera and Kauvar<sup>21</sup> reported 3 cases of acute temporal arteritis from the Peter Bent Brigham Hospital. This brings the number of cases reported in the literature to over 20. They point out that in temporal arteritis the presenting symptom is usually a severe, boring headache referable to both sides of the head, often severer on one side than on the other. Often, too, the pain is more intense at night, and frequently neither morphine nor barbiturates succeed in abolishing the pain. The temporal regions and temporal arteries may be tender, and during the course of the illness the vessels may become enlarged, tortuous and surrounded by areas of hyperemia. Tenderness and painful mastication were prominent features in one of the cases reported. The severity of the illness is often entirely out of proportion to the degree of local disease present. These authors suggest that the inflammation of the temporal artery is perhaps but a local manifestation of a more widespread disease. The histologic findings on biopsied arteries in these cases were the same as those described above. It is interesting that from a practical standpoint the most effective treatment seems to be removal of a segment of the temporal artery. After such therapy, the headache is relieved, even though the fever and generalized symptoms may continue for weeks.

This local benefit from biopsy probably depends on section of the sympathetic nerves.

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 27411

#### PRESENTATION OF CASE

A thirty-year-old single American woman was admitted to a mental hospital, where she remained until her death twenty years later.

The patient's family and personal histories were irrelevant. Her birth, infancy and early childhood were normal. She entered school at six and was considered very bright, but began to show a tendency toward seclusiveness and did not make friends easily. She enjoyed quiet, solitary diversions, was extremely sensitive, did not care for the company of men, and never had any love affairs. At the age of nineteen, the patient showed a definite change in her behavior: she cried a great deal, and was unable to give any reason for the change. At times she was hysterical, and could not control herself. This condition became progressively worse, and she began to lose interest in things she had previously liked. Finally, she would not talk at all. She then began to smile and laugh to herself, mumbled and spoke incoherently in low tones, and for several years would not converse. At the age of twenty-one, a panhysterectomy was performed on the recommendation of a psychiatrist. There was no further change in her general condition except that she gained about 100 pounds in weight. It was stated that until approximately one year before admission she was impulsive, violent and destructive. From the time of her institutionalization, when her physical and neurologic examinations were negative, until her death twenty years later, she showed progressive deterioration and reduction of activities. Eight years before death, the patient acted as if she had pain and tenderness in the gall-bladder region, and there were clay-colored stools. These symptoms persisted for a few weeks, then passed uneventfully. Two years later, the patient was placed on a diet and lost 85 pounds, the eventual weight being 165 pounds. Her condition was unchanged, and her general health appeared excellent. She was entirely out of communication with her physicians, mumbled to herself, fidgeted, and played with trinkets and toys. A Graham test showed no visualization of the gall bladder, but the examination was not

considered entirely satisfactory because of the large size of the patient and her general lack of co-operation. At this time, roentgenographic studies showed kidney outlines well visualized on both sides and normal in size, shape and position. Low in the pelvis on the left side, there were four small rounded areas of calcification, which had the appearance of phleboliths. Overlying the upper pole of the left kidney there was a group of irregular dense shadows, which could have represented renal calculi or calcified mesenteric lymph nodes. Repeat studies one year later again showed these several areas of density in the soft tissues, which were thought probably to represent calcified mesenteric nodes. No masses were felt on physical examination. The patient's condition remained approximately unchanged.

Eighteen months before death, the patient had, for the first time, an epileptiform convulsion accompanied by incontinence of urine and feces. The convulsion was generalized, and following it the patient seemed confused and drowsy. There were no definite neurologic findings, and no apparent headache, papilledema, stiff neck or localizing signs.

An electroencephalogram was suggestive of a pathologic process in the left occipitoparietal region. X-ray films of the skull were unusual but not definitely informative. There was irregular thickening of the inner table of the frontal bone, owing to hyperostosis, with unusually extensive calcification of the falx, but without evidence of chronic intracranial pressure.

Fifteen months before death, during the course of a routine physical examination done at the mental institution, an abdominal mass about 5 cm. in diameter was noted in the right lower quadrant. It was considered to coincide with the position of the calcified areas of density observed by x-ray study, and no further diagnostic procedures were attempted. On rectal examination, an extrinsic mass was felt about 5 cm. above the anus. Subsequent examinations showed several masses, about the same size, all palpable, and apparently increasing in size. Repeat stool examinations were negative for occult blood, the last test being done nine months before death.

The patient's condition continued with very little change until about six months before death, when she began to seem weak, and appeared to favor her abdomen as though there were pain or tenderness there. She vomited several times. There was no fever, and no constipation. The abdominal masses seemed somewhat larger. She failed gradually, showing physical deterioration. One month before death, she had "difficulty" with

respiration and developed a temperature of 102 to 104°F. Examination of the chest revealed dullness to flatness at the right base, with diminished breath sounds, and a roentgenogram taken with a portable machine showed evidence of fluid in the right pleural cavities and a linear band of density in the lung field, extending down from the right hilus.

The temperature from this time continued to fluctuate between 98.6 and 102.0°F., and physical findings in the chest increased; the patient be-

cannot remember ever to have heard of attempts to cure insanity by such an operation as this. It is very unfortunate that we do not know the details of the operation, since the term "panhysterectomy" has been applied to different operations at different times. As used today, it means that the uterus and tubes were removed and the ovaries were left behind. In 1910, I should suppose that it meant that the ovaries had also been removed. I think we can assume that the menses ceased, since we are given no information about

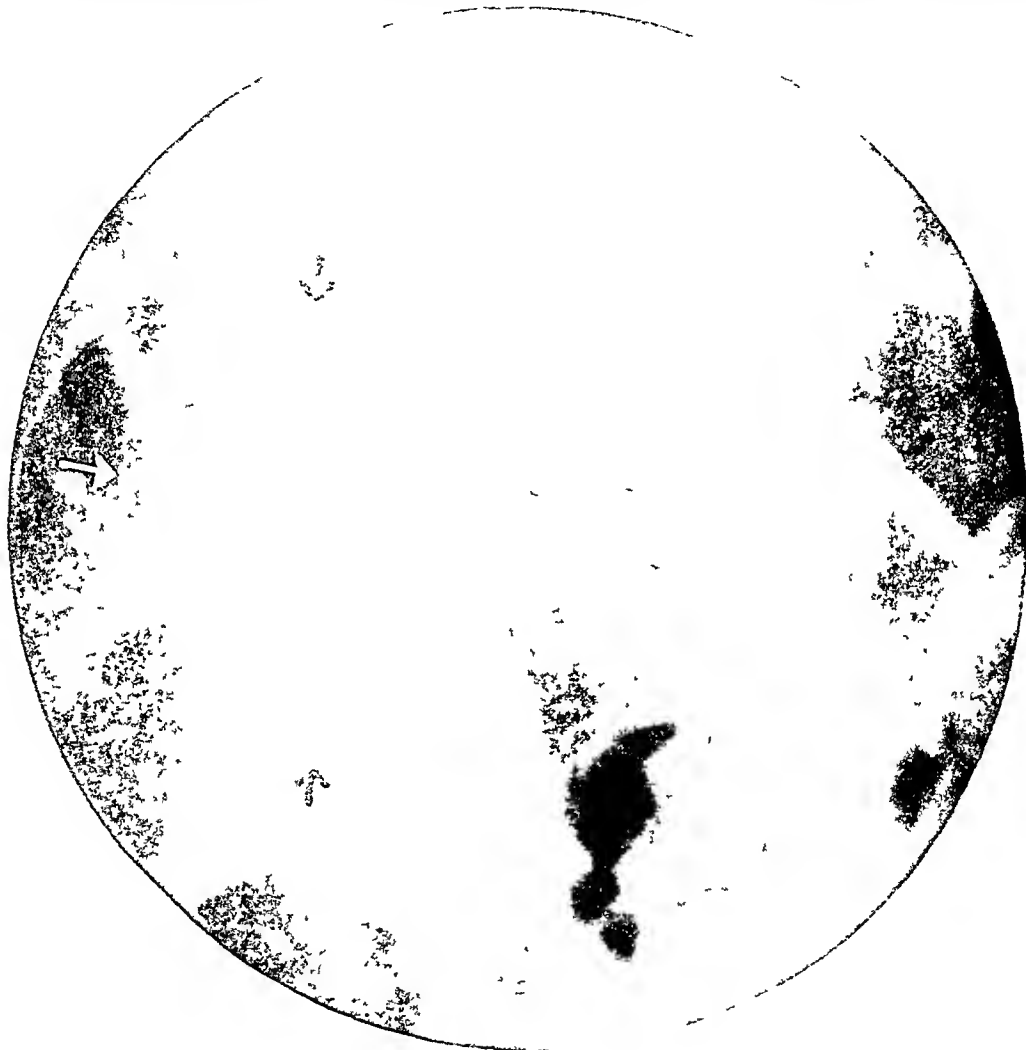


FIGURE 1. *Intravenous Pyelogram Showing Calcified Masses Superimposed on the Right Kidney Shadow.*

came weaker and developed mild dyspnea. She remained about the same for three weeks, and then quickly failed and died.

#### DIFFERENTIAL DIAGNOSIS

DR. JOE V. MEIGS: It would be presumptuous for a surgeon to attempt to discuss what kind of insanity this patient suffered from. It is evident even to the layman, however, that it was a major psychosis that demanded institutionalization. I

them. The insanity naturally made it impossible to inquire in detail about subjective symptoms such as periodic sensations in the breast and hot flashes, which would allow us to guess whether or not an artificial menopause was produced. It is obviously of great importance to know whether or not the ovaries were removed. I shall guess that they were, and am basing this assumption chiefly on the fact that the patient gained 160 pounds in a brief period after the operation. Of course, one can gain a great deal of weight after

any operation. One feels better and eats better, and the operation is an excuse for not exercising. However, a weight gain of 100 pounds is a striking phenomenon and definitely suggests that endocrine function was disturbed.

The gall bladder symptoms are reported to have persisted only a few weeks, they then passed uneventfully. This seems to me important because we are looking for all possible sites of primary neoplasm, to explain the subsequent history. But since the symptoms lasted only a few weeks, since we know that an unsatisfactory Graham test was later performed, and since the patient lived six years after the attack, I believe that there was nothing of serious consequence in the right upper quadrant. A report of an x-ray examination at this time suggested calcified mesenteric lymph nodes on the left side of the pelvis.

DR JAMES R. LINGLEY: This is the plain abdominal film taken six years before death. Low in the pelvis on the left, some small round areas of calcification, which at the time we thought were phleboliths, are visible. Higher up on the same side is a larger group of dense shadows that overlie the upper pole of the left kidney, these could be but probably are not renal calculi. They could be calcified mesenteric nodes. These films were taken six years later, and between the two examinations a remarkable change in the appearance of the abdomen had occurred. Unusually large areas of calcification were scattered throughout the abdomen. Here is one in the mid pelvis, which appears to form the upper border of a soft tissue mass. Another in the right upper quadrant has somewhat the appearance of a staghorn calculus. It lies outside the kidney outline, however, and above it (Fig 1). Here in the mid line is a large mass, which runs parallel to the transverse colon but was shown by a barium enema to be definitely outside the bowel. It was fairly movable, and we assumed that it was in the mesentery. In all these areas, the type of calcification is very unusual. It does not have the appearance of solid calcium but looks more as if the calcium were deposited in innumerable small particles throughout the soft tissue masses.

DR MEIGS: That was a great change—much greater than I had realized on reading the history. I note that they speak of a mass 5 cm in diameter, which was felt in the pelvis. That is only about the size of a golf ball, and if they could feel it in a patient who weighed 165 pounds it was probably even larger. The statement that repeated stool examinations were negative for blood is very important, and permits us to rule

out a primary tumor of the bowel. Evidently in the last few months the masses in the abdomen grew rapidly, and the patient began to go downhill, finally developing what might have been pneumonia, fluid in the chest or empyema. We are at a great disadvantage in not knowing certainly whether any ovarian tissue was left. If she still had her ovaries, one might think of a tumor primary in the upper abdomen, starting at about the time that she had the right upper quadrant difficulty, that metastasized to the ovaries and filled them with tumor analogous to a Krukenberg tumor. One also thinks of the possibility of a primary ovarian tumor, with metastases throughout the abdomen, including the omentum, this would account for the movable mid line tumor. Malignant ovarian tumors, particularly papillary adenocarcinomas, not infrequently undergo extensive calcification. Certainly that possibility cannot be ruled out. I have already committed myself, however, to the assumption that both the ovaries were taken out at the original operation. I do not know of any other neoplasms that calcify as extensively as this, and I must therefore fall back on the diagnosis of tuberculosis. I do not recall ever having seen a case of abdominal tuberculosis that progressed like this, but it remains my best guess and on that basis I assume that the final episode in the chest was probably a tuberculous pleurisy.

DR TRACY B. MALLORY: What would you say about the probability of tuberculosis, Dr Holmes?

DR GEORGE W. HOLMES: I am familiar with this case and consequently cannot give an unbiased opinion. I should like to point out that these are very unusual shadows. I cannot remember ever to have seen anything like this picture. Certainly it is not typical of tuberculosis.

DR WILLIAM RICHARDSON: I saw this patient two or three times and made a diagnosis of "rocks" in the abdomen of unknown etiology. The clinician who saw her placed most emphasis on the possibility of tuberculous etiology, but I think almost everyone was very much confused about the diagnosis.

#### CLINICAL DIAGNOSES

Schizophrenia  
Malignant disease, undetermined?  
Tuberculosis of retroperitoneal lymph nodes?

#### DR MEIGS'S DIAGNOSES

Tuberculosis of the abdominal lymph nodes  
Tuberculous pleurisy

## ANATOMICAL DIAGNOSES

Papillary cystadenocarcinoma of the ovary, with carcinosis of peritoneum and pleura and metastases to serous coats of intestines, liver, spleen and gall bladder.

Cardiac infarction.

Mural thrombus, right ventricle.

Pulmonary thrombus, left lower lobe.

Pulmonary infarct, left lower lobe.

Pulmonary atelectasis, bilateral, marked.

Hydrothorax, bilateral, marked.

(Schizophrenia.)

(Epilepsy.)

Frontal exostosis.

Ossification of falx cerebri.

Cholelithiasis.

Cortical cysts of kidney.

Hydronephrosis, left.

Hydroureter, left.

Operative scar: hysterectomy.

## PATHOLOGICAL DISCUSSION

DR. MALLORY: The autopsy proved one thing definitely—that it was not tuberculosis but metastatic tumor. All these tumor masses were extensively calcified. The calcification was mostly of a fine gritty character; gross examination suggested the type of calcification that is not infrequently seen in certain ovarian tumors and is due to very minute spherical masses of calcium known as psammoma bodies. When the microscopic sections came through, it was evident that the tumor was a papillary adenocarcinoma exactly similar in appearance to those that arise in the ovaries, with a great many psammoma bodies in it. It had metastasized very widely. We found many nodules scattered over the mesentery and on the bowels; apparently, these had started on the serosa and worked inward, some actually reaching the mucosa and almost obstructing the lumen. There were pleural metastases, which probably accounted for the chest fluid. The pelvis was totally filled with tumor material, and multiple sections at very close intervals failed to show anything that could be recognized as uterus, tubes or ovaries. If it were not for the story of the "panhysterectomy," I should assume that this was an ovarian tumor. We found no other probable primary site, and I have not happened to see a tumor of this type arising in any other tissue. Apparently, death was not due to the tumor but to a combination of a large infarct of the heart and pulmonary embolism. The skull showed extensive hyperostosis of the frontal bone, and the brain was grossly normal.

DR. MEIGS: I have seen ovarian tumors with calcification visible on x-ray films but never with as diffuse calcification as in these films. I should expect to see small granular areas more widely scattered.

DR. LINGLEY: We have seen another case with areas as close as these.

## CASE 27412

## PRESENTATION OF CASE

A sixty-two-year-old American schoolteacher was admitted complaining of marked breathlessness.

The patient had frequent sore throats until fourteen years before entry, at which time a tonsillectomy was performed. Subsequently, she had no recurrences. For about twenty-six years she had been slightly breathless on ordinary exertion, although this had not prevented her from carrying on her usual activities. For about five or ten years she had been aware of an irregularity of her heart, which had not been troublesome, however.

The irregularity had been constant so far as she knew. Four years before entry, she was seen by a physician because of bronchitis and was told that she had heart trouble and that her systolic blood pressure was 180. She was advised to take Digitora, one grain twice daily, which she continued to do until the time of entry. In spite of the treatment, the dyspnea had become more pronounced. Six months before admission, the patient consulted a physician for recurrent attacks of "intestinal flu," which were characterized by lower abdominal pain and nausea. The attacks were sufficiently severe to require rest in bed for a few days and sedatives for relief. They recurred at intervals for a few days to several weeks, but for the previous few months they had become less frequent and less severe. There was no associated vomiting, diarrhea or melena. Since the onset of this symptom, dyspnea had become more marked, and the ankles became swollen toward evening. For about four weeks, there were nocturnal attacks of dyspnea, associated with wheezing, which caused her to sit up in bed for relief. Occasionally, she was compelled to sleep in a sitting position. There was slight cough but no bloody sputum, and concomitant with the orthopnea there were a sensation of distress over the anterior chest and a tight feeling across the upper abdomen. For four days, there was marked swelling of the feet and legs up to the mid-thigh. There had been no previous attacks of rheumatic fever, chorea or related diseases.

Physical examination showed an elderly woman



propped up in bed, with slight cyanosis of the lips, face, fingers and hands. There was distention of the neck veins up to the angles of the jaw. A slight wheezing sound with respiration and occasional attacks of a Cheyne-Stokes type of breathing were noted. The apex impulse was diffuse and heaving, its maximal point being in the fourth interspace, 13 cm. to the left of the mid-sternal line. No thrills were palpable. The left border of dullness was 14 cm. from the mid-sternal line in the fourth interspace, 18 cm. in the third; the right border of dullness was 5 cm. in the fourth interspace. The rhythm was totally irregular, with an apical rate of 100. The pulse at the wrist was 60. The aortic second sound was moderately diminished, and the pulmonic was louder than the aortic and moderately accentuated. The first sound at the apex was marked by a moderate to loud, rather high-pitched systolic murmur, which was widely transmitted. At the apex, there was a short rumbling diastolic murmur immediately following the second sound. The blood pressure was 195 systolic, 110 diastolic. The radial arteries were soft, and the pulse moderately small in volume. Over the right lung base posteriorly, there were dullness and diminished to absent tactile fremitus. The breath sounds were diminished in intensity, but the voice sounds were of good quality. Throughout both lung bases, there were a moderate number of medium crepitant rales. The abdomen was soft, and the liver edge, which extended to the level of the umbilicus, was slightly tender. The spleen was not felt, and there was no evidence of ascites. There was edema of the lower extremities up to the mid-thigh.

The temperature was 100°F., and the respirations were 28.

Examination of the urine showed a specific gravity that varied between 1.008 and 1.014, with a slight trace of albumin. The sediment contained a rare red blood cell, 25 to 50 white blood cells and occasional granular casts per high-power field. The blood showed a red-cell count of 4,900,000 with a hemoglobin of 80 per cent, and a white-cell count of 10,000 with 73 per cent polymorphonuclears. A stool examination was negative. The blood Hinton reaction was negative. An electrocardiogram showed auricular fibrillation, with a tendency to right-axis deviation. There was low voltage and slurring of the QRS waves. T<sub>1</sub> was low; almost flat, and T<sub>2</sub> and T<sub>3</sub> low, with sagging ST intervals. Q<sub>4</sub> was 2 mm., and T<sub>4</sub> low and diphasic.

Three days after entry, shortly after a light lunch, the patient suddenly developed abdominal

discomfort and pain. This was relieved by a medicated enema, but shortly after its return, the patient became nauseated and vomited and her skin became ashen. She complained of epigastric discomfort and perspired freely. The blood pressure at that time was 200 systolic, 100 diastolic. There was an increase in moist rales in the chest, and the sputum was faintly tinged with bright-red blood. About fifteen minutes later, this attack subsided, but the patient continued to bring up streaked sputum for the next few days. Despite the administration of digitalis and sedatives, the patient's general condition remained unchanged, and the heart rate was not lessened. There was dyspnea at rest, and the cyanosis and engorgement of the neck veins continued. On the tenth hospital day, a right thoracentesis was performed, and 1360 cc. of straw-colored fluid withdrawn. This closed before the procedure was completed. Immediately after the tap, the patient stated that a constricting sensation, from which she had previously suffered, had subsided. Subsequently mercurial diuretics were administered, and the patient became more comfortable, although additional chest taps were necessary.

One month after entry, it was noted that nocturnal dyspnea was increasing in frequency and severity. Throughout this time, the temperature fluctuated between 98 and 101°F. Increasing dosage of digitalis failed to control the ventricular rate completely, and a pulse deficit of 40 to 80 continued. Blood-stained sputum was frequently noted. About ten weeks after entry, the patient was suddenly seized with a shaking chill and became markedly cyanotic, and the pulse at the wrist was imperceptible. She was more comfortable shortly afterward, although the temperature rose to 102°F. Three days later, note was made of pain across both sides of the upper abdomen, radiating to the back. The apical heart rate rose to 120, and there was an icteric tint to the scleras. At this time, the white-cell count was 30,000, with 89 per cent polymorphonuclears. The icteric index was 70. The nonprotein nitrogen of the blood was 38 mg. and the serum protein 4.4 gm. per 100 cc. Her condition remained essentially unchanged for the succeeding two weeks, and at that time copious spitting of blood began. This was associated with a slight cough, and the blood apparently welled up in the throat. The expectorated material was almost pure blood, with very little mucus. There was no dyspnea or jugular engorgement, but numerous moist rales were audible throughout both chests. Subsequently, her condition became progressively worse, and she died three months after entry.

## DIFFERENTIAL DIAGNOSIS

DR. EDWARD F. BLAND: Here is a woman who had been mildly incapacitated by shortness of breath, presumably referable to her heart, for twenty-six years, from the age of thirty-six to sixty-two, and with irregularity of the heart for the last ten years of her life. We know that it was fibrillation ultimately, and the terminal events consisted in congestive failure and certain complications thereof. I know of but one type of heart disease that is apt to permit such a long life with moderate disability for so many years—rheumatic heart disease. Irrespective of the physical signs, I think we can be reasonably certain of this on the basis of the history alone. From the physical signs described, the patient undoubtedly had extensive involvement of the mitral valve, with regurgitation and stenosis. There was, of course, marked enlargement of the heart. Most of the other signs described are consistent with rheumatic heart disease and heart failure. I suppose that an x-ray film was taken. She could hardly have been in the hospital for three months, with all these things happening, without a chest film. I should be interested in that.

DR. BENJAMIN CASTLEMAN: No x-ray films were taken.

DR. BLAND: Perhaps the patient was too sick. It would have been of interest to search for calcification of the mitral valve. There probably was some, but it might have shown up only under the fluoroscope, or perhaps not even there. It would have been of further interest to know if we were dealing with something other than cardiac impairment as a contributing cause of the long-standing dyspnea.

The electrocardiogram is of some interest. It shows a little right-axis deviation; I should have expected more. Of course, this patient also had hypertension, which imposed an added strain on her heart, principally on the left ventricle, and hence would tend to lessen the degree of right-axis deviation that she might otherwise have had. The description in the record covers satisfactorily the other electrocardiograms shown here on the screen. There was auricular fibrillation, rather low voltage and very slight right-axis deviation, the degree of which, as noted above, is a little disturbing. There was also a digitalis effect on the T waves, although, as we shall note shortly, the ventricular rate was controlled only with a good deal of trouble.

I should like to speculate a little about the probability of slight scarring of the aortic valve in the presence of such extensive rheumatic involvement of the heart. Nothing in the physical signs de-

scribed permits one to guess that such scarring occurred, but I think that there is perhaps a fifty-fifty chance of finding a relatively slight degree of aortic-valve involvement.

Certain features of the final illness require some special consideration, and I think there may be some reasonable difference of opinion concerning them. The attacks, called abdominal, before she came to the hospital interest me. They coincided with the beginning of frank congestive failure and consisted in pain and nausea, without other gastrointestinal symptoms. We know that pain in the abdomen with congestive failure is common and most frequently due to demonstrable engorgement of the liver. Sometimes, people have pain from a sore liver oftener at night than during the day, probably because of the semirecumbent position assumed in bed, whereas when they sit in a chair the liver is not quite so encroached on. For a number of years, we have been searching without success for an explanation of the abdominal pain when congestive failure is not evident in patients with well-marked mitral stenosis. Here we need, I think, look no farther than to the congestion of the liver and of the gastrointestinal tract as a satisfactory explanation. Mesenteric embolism seems unlikely.

We now come to a second point, which I think needs a little discussion. These recurring episodes of pulmonary distress, which were associated with an increase in the signs of congestion and one of which was accompanied by an actual chill, together with the vague pain in the chest followed by fever, hemoptysis and icterus, were certainly due to multiple pulmonary infarction. This patient had two very good reasons for having both respiratory distress and hemoptysis. She had obvious congestion of the lungs, and she might have had a little blood in the sputum simply from this. However, these recurring episodes, especially the one followed by icterus, indicate multiple pulmonary infarcts. The degree of icterus in this patient is interesting, for an icteric index of 70 represents considerable jaundice and hence extensive infarction, I should guess. Someone asked me recently if we saw icterus as a result of infarction of organs other than the lungs. At the time, I did not recall such a case.

DR. CASTLEMAN: We have had one case of jaundice associated with infarction of the heart without pulmonary infarction. It was reported several years ago.<sup>1</sup>

DR. PAUL D. WHITE: Yes; I remember that case. I suppose that such a case is related to the extent of hemolysis and the passive congestion in the liver.

DR CASTLEMAN Yes, both factors must be present

DR BLAND The next point I should like to comment on is this patient's fever. There are several adequate reasons why she may have had fever. Extensive congestive failure may give rise to a degree or two. We know that the pulmonary infarcts could have caused fever, but the question is raised whether any other infection was present, bacterial or otherwise. Perhaps not, but I shall keep that possibility in mind for a final word later.

Toward the end of her life, the patient had a low serum protein, 4.4 gm per 100 cc, which is within the edema range. She had several obvious causes for a low serum protein. Undoubtedly, the dietary intake for one reason or another had been inadequate. She had congestion of the liver and had lost fluid by both diuresis and tapping. All these factors might have contributed. Then we come to the question of some obscure infection in the heart as a possible added factor in her demise. In a young person, heart failure complicating a rheumatic heart is a fairly reliable sign of underlying infection of some sort or other, but this patient was too old to apply this general principle without other supporting evidence, so that we have to discount the presence of congestive failure as a possible indication of active infection, bacterial or rheumatic. A good deal of difficulty was obviously encountered in controlling the ventricular rate. Among the things in general that make it difficult to control the ventricular rate when fibrillation is present are infection, infarction in the lung and thyrotoxicosis. There is no reason to suspect thyrotoxicosis. I think that the patient had multiple infarction of the lungs which is probably the best explanation.

A final word about the lungs. I was puzzled why the patient bled so much from her lungs at the end, since there was not much evidence at that time of gross congestion and since, in fact, the pulmonary congestion seemed temporarily better, yet she raised almost pure blood, without sputum and with very little cough. That is a little unusual, but perhaps the pulmonary circulation was better because she was raising blood. We know that patients with rheumatic heart disease and mitral stenosis are prone to bleed from the lungs from either infarction or congestion and at times without clinical evidence of either. I think it unlikely that Dr. Castleman will tell us later that the patient had a rheumatic pneumonitis. Although I do not like to discard it without some further comment, I do not believe I could make a diagnosis of acute rheumatic fever.

Did she have bacterial endocarditis? I do not believe so for several reasons. She had auricular fibrillation. That does not exclude endocarditis, but the combination is a little unusual. She had chronic congestive failure for at least nine months. That would be most unusual if the heart failure were due to bacterial infection. Did she have some chronic disease of the lung to explain her respiratory symptoms rather than chronic heart disease? Probably not. She had respiratory symptoms for too many years, with no clubbing of the fingers and no suggestive sputum during that time.

In summary, I should say that in spite of the patient's age she had chronic rheumatic heart disease, with extensive mitral involvement, both stenosis and regurgitation. She had a complicating hypertension, which may have been an added factor in the later downhill course and ultimate death, but the rheumatic disease of the heart was, I believe, of first importance. She died of chronic congestive heart failure, with recurring pulmonary emboli and infarction.

DR HOWARD B. SPRAGUE Abdominal pain in these patients with cardiac failure bothers me as much as it does Dr. Bland. Some of them who do not have much enlargement of the liver may have acute engorgement causing pain. Also, we have been surprised to find renal infarcts in these patients. I want to ask Dr. Castleman, Is it possible to get small enough emboli to the blood supply of the intestines to have attacks of pain without infarction of the intestinal wall?

DR CASTLEMAN I do not believe so. Infarction is found only when the larger vessels are occluded, because ordinarily there is enough collateral circulation between the intestinal branches to prevent it. I suppose emboli in the mesenteric branches are not uncommon, but I do not believe they have been hunted for seriously enough.

DR WHITE With reference to renal infarction, Dr. Reno R. Porter and I<sup>2</sup> found that renal infarcts are usually painless. The majority of patients whom I have seen with abdominal pain complicating heart failure have had distention of the intestine from gas due, in part at least, to stasis. They usually have liver engorgement also, but not always. Of course there is some thing here besides <sub>3, 15</sub>

#### CLINICAL DIAGNOSES

Valvular disease, chronic, cardiac  
Mitral stenosis  
Hypertension  
Pulmonary infarction

## DR. BLAND'S DIAGNOSES

Rheumatic heart disease.  
Mitral stenosis and regurgitation.  
Auricular fibrillation.  
Congestive heart failure.  
Multiple pulmonary infarcts.  
Hypertension.

## ANATOMICAL DIAGNOSES

Rheumatic heart disease, chronic, with mitral stenosis.  
Cardiac hypertrophy.  
Mural thrombus, left auricle.  
Thrombosis of popliteal vein, left.  
Pulmonary embolism, bilateral.  
Pulmonary infarction, right lower lobe.  
Icterus.  
Renal infarction, multiple, bilateral, healed.  
Arteriosclerosis, marked aortic, moderate coronary.  
Nephritis, chronic vascular, marked.  
Chronic passive congestion of liver and spleen.  
Pulmonary congestion.  
Hydrothorax, bilateral.  
Peripheral edema.  
Peritonitis, chronic fibrous.  
Cholelithiasis.  
Dilatation of bile ducts.  
Focal necrosis and abscess formation of pancreas.

## PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: This patient had a large heart, weighing 800 gm., with marked dilatation and hypertrophy of the right auricle and ventricle. The right ventricle measured 5 mm. in thickness, which I think would be enough to cause right-axis deviation.

DR. BLAND: It is not entirely a question of the thickness. It is a question of disproportion between the normal ratios of the two ventricles.

DR. CASTLEMAN: The left measured 17 mm. The mitral valve was markedly stenotic and calcified, although the opening measured 3 cm. in circumference. In the left auricular appendage was a mural thrombus, and there were small healed renal infarcts that may have had something to do with the pain, but I doubt it. There were several large infarcts in the lower lobe of the

right lung involving about two thirds of the lobe; the other lobes were normal. The extent of the infarction, together with the congestion of the liver, certainly accounts for the icterus. There was about 200 cc. of fluid in the right pleural cavity, and 50 cc. in the left. In addition, old adhesions were found all over the abdomen, especially in the region of the gall bladder, which was filled with two large stones and inspissated bile. The pancreas showed several areas of acute fat necrosis, and I believe the abdominal pain was due to some disturbance in the biliary tract associated with chronic pancreatitis. Small foci of old fat necrosis are occasionally seen without symptoms, but here it was much more acute than usual.

DR. WHITE: Was there any active myocardial rheumatic disease?

DR. CASTLEMAN: No; we were unable to find any evidence of active rheumatic infection.

DR. BLAND: The aortic valve was not involved?

DR. CASTLEMAN: It showed a little calcification on the sinus side of the valve but no true inter-adherence. I think one would question whether there was any.

DR. BLAND: Was there any pericarditis?

DR. CASTLEMAN: No.

DR. SYLVESTER MCGINN: How about the leg veins?

DR. CASTLEMAN: The source of the infarct in the lung was the left popliteal vein. It is often supposed that the infarcts in the lungs in patients with fibrillation are due to mural thrombi in the right auricle, but if one examines the deep leg veins in those cases, another more likely source may be uncovered. In this case, the right auricle was normal.

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## Erratum

In Case 27331 of the "Case Records of the Massachusetts General Hospital" in the August 14 issue of the *Journal* (line 18, column 1, page 272), the word "aminophyllin" was used erroneously for aminopyrine. The speaker did not mean to imply that aminopyrine caused liver damage, but that it was an equally dangerous drug, the toxicity in this case being directed toward the granulocytes.

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## PUBLIC EDUCATION IN MEDICAL MATTERS

THE Diabetes Education Program that is being sponsored by the Metropolitan Life Insurance Company is an encouraging example of public interest in good medicine. The increasing evidence that the early recognition and careful control of diabetes are important in checking the progress of the pancreatic and neurovascular lesions makes such a program particularly timely.

The economic value of good health to such an insurance company is of course obvious. But good public health or that of the individual is of equal value to private enterprise. Loss of work due to ill health is an economic burden to almost all industry. The vast sums of money spent annually

by the American people on life and sickness insurance provide evidence concerning the value that they have long placed on life and health. Advances in medical science have so increased the effectiveness of available medicine that the public's interest is shifting from *insuring* health and life by cash indemnities to *securing* health and longevity by medical care. The expansion of health programs by state departments of public health and a variety of nonprofit lay organizations reflects the public's increasing appreciation of the effectiveness of modern medicine. The National Health Conference and the recent National Nutrition Conference were reflections of public awareness and interest. The federal government has responded through the programs of the United States Public Health Service, of the Maternity and Child Welfare Division of the Department of Labor, and of the National Health Institute at Bethesda, Maryland. This increased awareness is creating an increased demand for medical care. To finance this care, a variety of plans for voluntarily distributing and budgeting the costs of medical care are developing throughout the country. Although it is not widespread, there is even some demand for compulsory health insurance. Insofar as the layman's medical education is good and the plans for budgeted health services are sound, the medical profession, as well as the public, will benefit. The result should be more and better medicine more widely and, therefore, with present economic trends, better paid for in the long run.

So far so good, and the medical profession should indeed be happy. But there are, of course, many who will turn the public's interest in medicine to their personal advantage. For every educational program like that sponsored by the Metropolitan Life Insurance Company for better health, there will be one hundred programs on the radio and in the press sponsored by commercial organizations for the sale of unneeded or worthless medication. The same American advertising genius that has popularized alkalinizing, laxativizing and antihaltizing remedies apparently is taking over the newly cultivated fields of vitamin and hormone

therapy. As it does so, the money that the public should spend for effective health and medical services will be squandered to such an extent that sums spent on the trial-and-error method of establishing workable insurance schemes will seem inconsequential. But no matter what becomes of the money, the medical profession in the end will pay the bill, so the public will be happy anyway.

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## MEDICAL PATENTS

THE medical profession has always been imbued with the idea of the free exchange of knowledge gained from research. The meetings of our societies and the contents of our journals bear witness to this fact. The inauguration of medical patents in certain fields has cast a blight on this traditional ideal. Holders of medical patents are learning that the onerous duties of controlling and protecting their patents tend to cast disturbing shadows over the glory of discovery.

The Department of Justice recently chose to bring suit against three leading pharmaceutical manufacturers in the United States on the charge of fixing the price of insulin in violation of the Sherman Act. Heavy fines were imposed. The University of Toronto, holders of the patent, had granted licenses to these manufacturers to make and sell insulin. The Insulin Committee of this institution has apparently carried out its responsibilities concerning standards and prices of the product marketed in a manner satisfactory to the medical profession of North America, and this committee has never ventured to control research in the field of diabetes. The judgment, then, seems to be against the manner of price fixing rather than against the quality of the product or any unreasonable profit on the part of the manufacturers.

The emoluments received by the patentees in this case were beyond the scope of this judgment. At one time, the royalties on insulin were 10 per cent, whereas those on the Dick patent, held by a committee associated with the University of Chicago, were 5 per cent. Yet, on June 4, 1935, the Council of the Massachusetts Medical Society

adopted a resolution expressing disapproval of the Dick patent, the objection being based purely on the ground of the patentees' monopolistic control of investigative work in the field of scarlet fever.

Since patents appear to be necessary for the control of standardization of products in the existing situation, the control should lie with the highest tribunal of our medical councils or with the Government. The patents would then be dedicated to the public, and all royalties abolished in conformity with a tradition handed down from the days of Hippocrates. This suggestion was presented more than a year ago before the House of Delegates of the American Medical Association, but was set aside. It behooves the American Medical Association to renew its interest in the solution of this problem before federal authorities, probing farther into medical patents, charge organized medicine with lending support to a monopolistic practice that strikes at the very heart of academic freedom.

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## MEDICAL EPONYM

### Koch's POSTULATES

These postulates are laid down in the monumental contribution of Robert Koch (1843-1910), "Die Aetiologie der Tuberculose (The Etiology of Tuberculosis)," which was delivered as a lecture to the Physiological Society in Berlin on March 24, 1882. It appears in the *Berliner klinische Wochenschrift* (19: 221-230, 1882). A portion of the translation follows:

To prove that tuberculosis is a parasitic disease occasioned by the invasion of the bacilli and primarily caused by their growth and increase, these bacilli had to be isolated from the body, and kept in pure culture until they were free from any possible contamination with other disease products of the animal organism; and finally it was necessary to reproduce the same disease picture of tuberculosis (which experience showed could be obtained by injection of naturally produced tuberculous material) by transfer of the isolated bacilli into animals.

Koch then described his method of staining the tubercle bacilli, finding them in the lesions and culturing them. His success in reproducing tuberculous lesions and recovering the bacilli from them established a standard for this type of bacterial investigation that has remained fixed ever since.

R. W. B.

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SECTION OF OBSTETRICS  
AND GYNECOLOGY\*ALBUMINURIA AND HYPERTENSION FOLLOWED  
BY POST PARTUM ECLAMPSIA AND DEATH

A thirty-one year-old para III was seen in the fifth month of pregnancy for the first time. Following that, she was seen by the district nurse quite frequently.

The past history was not remarkable. Physical examination at the time of her visit to the physician was reported to have been negative.

Six weeks before delivery, the patient had a systolic blood pressure of 150. During the next month, she was seen ten times by the district nurse, who found that the systolic blood pressure averaged from 150 to 200 and that there was a trace of albumin in the urine. The attending physician was notified of these findings. The patient started in spontaneous labor at term and delivered herself of a living child. An hour later, several severe convulsions occurred. The patient was sent to the hospital and died approximately one day after delivery, without regaining consciousness.

*Comment.* Albuminuria and increased blood pressure during pregnancy, and convulsions following delivery, still occur in this day of enlightened medicine. There is no reason to suppose that this death was unavoidable. Any conscientious practitioner, when notified that a patient had a systolic blood pressure of 200 and a trace of albumin a few weeks before the expected date of delivery, would have done something about the situation. Such a patient should be hospitalized and intensively treated by a milk diet and milk of magnesia, salt should be omitted from the diet. If the blood pressure does not come down, labor should be induced, thus preventing a fatality. This case is a disgrace to the medical profession.

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Tuttle, Secretary, 230 Dartmouth Street, Boston.

## APPLICANTS FOR FELLOWSHIP†

PUBLISHED IN ACCORDANCE WITH THE PROVISIONS OF THE BY LAWS (CHAPTER V, SECTION 2) AS AMENDED MAY 22, 1941.

## BARNSTABLE DISTRICT

ROBINSON, JOSEPH, 25 Barnstable Road, Hyannis  
Middlesex University School of Medicine, 1933 Sponsor  
Frank Travers, Kings Highway, Barnstable.

Some of these applications were received too late under the By Laws of the Massachusetts Medical Society to be considered at the annual examination on December 1.

SANBORN, FREDERICK, Barnstable County Sanatorium, Pocasset.

Harvard Medical School, 1937.

SOBEL, HARRY, 55 Winter Street, Hyannis  
Middlesex University School of Medicine, 1932 Sponsor  
Harold F. Rowley, Harwich Port.

TRIPP, EDWIN P., JR., Falmouth.  
Jefferson Medical College of Philadelphia, 1938.

Donald E. Higgins, Secretary  
Main Street, Cotuit.

## BERKSHIRE DISTRICT

CARPENTER, FREDERICK J., 199 Springside Avenue, Pittsfield.

McGill University Faculty of Medicine, 1936.

MCALPIN, KENNETH R., 29 Hoxsey Street, Williamstown.  
Columbia University College of Physicians and Surgeons, 1910.

George S. Reynolds, Secretary  
7 North Street, Pittsfield.

## BRISTOL NORTH DISTRICT

BEDINGER, ADA D., Taunton State Hospital, Taunton.  
University of Pennsylvania School of Medicine, 1939.

BELMONT, FRED R., 42 Summer Street, Taunton.  
University of Berlin, 1921 Sponsor William H. Swift, 141 High Street, Taunton.

BOYD, JAMES G., Taunton State Hospital, Taunton.  
Boston University School of Medicine, 1939.

HAMEL, ALBERT G., Taunton State Hospital, Taunton.  
Georgetown University School of Medicine, 1929.

William H. Swift, Secretary  
141 High Street, Taunton.

## BRISTOL SOUTH DISTRICT

BERNSTEIN, SIGMUND, 415 County Street, New Bedford.  
University of Vienna, 1909 Sponsor Charles A. Bonney, Jr., 41 Maple Street, New Bedford.

HAGIN, CORNELIUS E., JR., 229 Belmont Street, Fall River.  
Medical College of Virginia, 1935.

MAGNOLSON, PAUL L., 76 Cottage Street, New Bedford.  
New York University College of Medicine, 1937.

MOONEY, DANIEL L., 164 Colfax Street, Fall River.  
Harvard Medical School, 1937.

PICARD, JULIUS, 473 Walnut Street, Fall River.  
University of Heidelberg, 1921 Sponsor Samuel Brown, 130 Rock Street, Fall River.

SCHWARTZ, WILLIAM, 240 Second Street, Fall River.  
College of Physicians and Surgeons, Boston, 1934 Sponsor Thomas G. Clarke, 181 Purchase Street, Fall River.

SMITH, VERA L., Swansea.  
College of Medical Evangelists, 1937.

Albert H. Sterns, Secretary  
31 Seventh Street, New Bedford.

## ESSEX NORTH DISTRICT

KAPLAN, LOUIS S., Birch Road, Salisbury.  
Middlesex University School of Medicine, 1935 Sponsor Clarence R. Hines, 39 Market Street, Amesbury.

SCHLOMER, GEORGE M., Georgetown.

University of Munich, 1910. Sponsor: Harry C. Solomon, 270 Commonwealth Avenue, Boston.

SETTLAGE, ARNOLD F. E., 244 High Street, Newburyport.  
Harvard Medical School, 1933.

Harold R. Kurth, *Secretary*  
477 Essex Street, Lawrence

#### ESSEX SOUTH DISTRICT

EIGNER, SIDNEY, 16 Newhall Street, Lynn.  
Boston University School of Medicine, 1937.

NUSSBAUM, JULIUS, 291 Summer Street, Lynn.  
University of Vienna, 1925. Sponsor: Albert H. Covenor, 89 Broad Street, Lynn.

PALLOTTA, JOHN J., 76 Main Street, Essex.  
Kansas City University of Physicians and Surgeons, 1933. Sponsor: T. Herbert Foote, 2 North Main Street, Ipswich.

SARRIS, SPIROS P., 145 Lewis Street, Lynn.  
Harvard Medical School, 1936.

J. Robert Shaughnessy, *Secretary*  
24½ Winter Street, Salem

#### FRANKLIN DISTRICT

ADLER, ERIC D., 26 Congress Street, Greenfield.  
University of Heidelberg, 1913. Sponsor: Arthur H. Ellis, 58 Federal Street, Greenfield.

Harry L. Craft, *Secretary*  
Ashfield

#### HAMPDEN DISTRICT

BORFENSTEIN, MORRIS V., 285 Union Street, Springfield.  
University of Vienna, 1936. Sponsor: Joseph Hahn, 146 Chestnut Street, Springfield.

DAVID, LEO, 686 Sumner Avenue, Springfield.  
University of Berlin, 1919. Sponsor: Alfred M. Glickman, 1938 Main Street, Springfield.

DEFEO, AMADEO J., 5 Lincoln Place, Monson.  
Middlesex University School of Medicine, 1935. Sponsor: Aloria H. Genest, Chicopee Hospital, Aldenville.

EDELMAN, WALDO G. A., 30 Belmont Avenue, Springfield.  
College of Physicians and Surgeons, Boston, 1935. Sponsor: Charles L. Furcolo, 14 Maple Street, Springfield.

GINSBURG, DAVID, 505 Armory Street, Springfield.  
Midwest Medical College, 1934. Sponsor: Bernard F. Gilchrist, 293 Bridge Street, Springfield.

GROVER, NATHAN Z., 539 State Street, Springfield.  
Tufts College Medical School, 1939.

IZENSTEIN, LOUIS A., 132 Belmont Avenue, Springfield.  
University of Cincinnati College of Medicine, 1938.

JORCZAK, JOHN S., 250 School Street, Chicopee.  
College of Physicians and Surgeons, Boston, 1930. Sponsor: Kenneth S. Fletcher, 145 Springfield Street, Chicopee.

KLAR, J. JOSEPH, 124 Ellsworth Avenue, Springfield.  
College of Physicians and Surgeons, Boston, 1934. Sponsor: Richard E. Dickson, 598 Dwight Street, Holyoke.

MAZZOLINI, ANDREW, 274 Maple Street, Holyoke.  
Middlesex University School of Medicine, 1933. Sponsor: Arthur L. Kinne, 265 Maple Street, Holyoke.

SCHWARTZ, LEO, 110 West Alvord Street, Springfield.  
Middlesex University School of Medicine, 1934. Sponsor: James A. Seaman, 20 Maple Street, Springfield.

STEINHARDT, ARTHUR H., 120 Belmont Avenue, Springfield.

University of Goettingen, 1919. Sponsor: Bernard F. Gilchrist, 293 Bridge Street, Springfield.

WHITCOMB, AUSTIN E., 21 Bardwell Street, South Hadley Falls.

Columbia University College of Physicians and Surgeons, 1937.

Wayne C. Barnes, *Secretary*  
146 Chestnut Street, Springfield

#### HAMPSHIRE DISTRICT

BRICK, EDWARD J., 66 Roe Avenue, Northampton.  
Middlesex University School of Medicine, 1934. Sponsor: Joseph D. Collins, 187 Main Street, Northampton.

Joseph R. Hobbs, *Secretary*  
16 Center Street, Northampton

#### MIDDLESEX EAST DISTRICT

MARCOUX, WILLIAM G., 383 Upham Street, Melrose.  
Tufts College Medical School, 1939.

PROCHNIK, JAMES J., 19 Yale Avenue, Wakefield.  
University of Vienna, 1919. Sponsor: Hyman Morrison, 483 Beacon Street, Boston.

Kenneth L. MacLachlan, *Secretary*  
1 Bellevue Avenue, Melrose

#### MIDDLESEX NORTH DISTRICT

BOYNTON, GEORGE H., Billerica.  
Middlesex University School of Medicine, 1934. Sponsor: Daniel J. Ellison, 8 Merrimack Street, Lowell.

KARBOWNICZAK, JOHN J., JR., 465 High Street, Lowell.  
Middlesex University School of Medicine, 1936. Sponsor: Henry S. Glidden, State Infirmary, Tewksbury.

LANDAU, IRVING I., Boston Road, Billerica.  
University of Berlin, 1934. Sponsor: A. Warren Stearns, Boston Road, Billerica.

LEACH, HARRIET P., 23 Lowell Road, Chelmsford.  
Yale University School of Medicine, 1935.

ROSENBAUM, EMIL E., 617 Westford Street, Lowell.  
University of Berlin, 1915. Sponsor: Philip G. Beraman, 174 Central Street, Lowell.

SICARD, LOUIS A., 130 Avon Street, Lowell.  
Tufts College Medical School, 1940.

RAOUL L. DRAPEAU, *Secretary*  
310 Merrimack Street, Lowell

#### MIDDLESEX SOUTH DISTRICT

BLOOMENTHAL, ABRAHAM P., 5 Banks Street, Waltham.  
Middlesex University School of Medicine, 1934. Sponsor: Albert L. Barron, 666 Main Street, Watertown.

BROADHURST, ALICE M., 123 Barnard Avenue, Watertown.  
Tufts College Medical School, 1939.

CASEY, DAVID T., 131 Putnam Avenue, Cambridge.  
Tufts College Medical School, 1938.

CUTTER, EDWARD P., 3 Craigie Circle, Cambridge.  
Harvard Medical School, 1938.



- UTSCH, FELIX**, 44 Larchwood Drive, Cambridge  
University of Vienna, 1909 Sponsor John M. Murray, 82 Marlboro Street, Boston
- IRENTHIEL, OTTO F.**, 12 Priscilla Road, Brighton  
University of Vienna, 1923 Sponsor Hyman Morrison, 483 Beacon Street, Boston
- NOTE, ESTELLE**, Walter E. Fernald State School, Waverley  
University of Vermont College of Medicine, 1926
- ARTI, EMILIO**, 32 Commonwealth Avenue, Chestnut Hill  
Royal University of Modena, 1924 Sponsor Morton S. Stern, 371 Commonwealth Avenue, Boston
- OLDBERG, JOSEPH**, 384 Ferry Street, Malden  
Middlesex University School of Medicine, 1929 Sponsor Max M. Braff, 37 Princeton Street, East Boston
- AINES, GEORGE A.**, 641 Broadway, Everett  
Middlesex University School of Medicine, 1915 Sponsor James F. Burns, 537 Broadway, Everett
- UEBER, JOHN W.**, 25 Day Street, West Somerville  
Tufts College Medical School, 1939
- OPANS, DAVID E.**, 20 Belmont Street, Newton  
Harvard Medical School, 1938
- OWAL, ANNE H.**, Walter E. Fernald State School Waverley  
University of Michigan Medical School, 1938
- EVI, PAOLO**, 84 Salisbury Road, Watertown  
University of Milan, 1928 Sponsor Andrew W. Conratto, 99 Bay State Road, Boston
- YONS, ARTHUR W.**, 202 Washington Street, Brighton  
Tufts College Medical School, 1938
- JACKLIN, JAMES J., JR.**, 12 Crescent Street, Cambridge  
Tufts College Medical School, 1940
- FEINHARDT, CHARLES**, 271 A Salem Street, Malden  
College of Physicians and Surgeons, Boston, 1935  
Sponsor Louis Silver, 483 Beacon Street, Boston
- IERZBACH, PETER F.**, 3 Sacramento Street, Cambridge  
University of Frankfurt, 1933 Sponsor Louis Zetzel, 53 Bay State Road, Boston
- VEHVALSER, EDWARD B. D.**, 10 Shady Hill Square, Cambridge  
University of Pennsylvania School of Medicine, 1934
- BRNSTEIN, FRANK E.**, 223 Park Avenue, Arlington  
University of Vienna, 1920 Sponsor Harry C. Solomon, 270 Commonwealth Avenue, Boston
- RICHARDS, HAZEL H.**, 234 Main Street, Malden  
Middlesex University School of Medicine, 1930 Sponsor Russell F. Sullivan, 1101 Beacon Street, Brookline
- ROTTSCHILD, KARL**, 11 Parker Street, Malden  
University of Munich, 1915 Sponsor Benjamin F. Sieve, 371 Commonwealth Avenue, Boston
- SLATE, BENJAMIN**, 156 Line Street, Cambridge  
Middlesex University School of Medicine, 1935 Sponsor Louis Albert, 45 Bay State Road, Boston
- STELLAR, LAWRENCE I.**, 58 Cloverdale Road, Newton Highlands  
Tufts College Medical School, 1938
- SULZBACH, WOLFGANG M. F.**, McLean Hospital, Waverley  
University of Bonn, 1935 Sponsor Kenneth J. Tillotson, McLean Hospital, Waverley
- WHITE, THOMAS P.**, 67 Cherry Place, West Newton  
Tufts College Medical School, 1937
- WIES, DAVID**, McLean Hospital, Waverley  
Tufts College Medical School, 1935

Alexander A. Levi, *Secretary*  
481 Beacon Street, Boston

## NORFOLK DISTRICT

- ALLEN, F. HAROLD, JR.**, 300 Longwood Avenue, Boston (Roxbury)  
Harvard Medical School, 1938
- BELL, SOLOMON Z.**, 428 Park Street, Dorchester  
Middlesex University School of Medicine, 1934 Sponsor Fred Finkle, 37 Columbia Road, Dorchester
- BENNETT, NATHANIEL N.**, 174 Harvard Street, Brookline  
Middlesex University School of Medicine, 1934 Sponsor Mark Falcon Lesse, 375 Commonwealth Avenue, Boston
- COHN, ERNST**, 39 Columbia Road, Dorchester  
University of Wuerzburg, 1922 Sponsor Isadore Olef, 371 Commonwealth Avenue, Boston
- HOFFMAN, RICHARD**, 327 St. Paul Street, Brookline  
University of Vienna, 1920 Sponsor Samuel L. Gargill, 474 Beacon Street, Boston
- LEVY, DUBORAH C.**, 44 Burroughs Street, Jamaica Plain  
Yale University School of Medicine, 1936
- LEONARD, PAUL C.**, 62 Bowdoin Avenue, Dorchester  
Tufts College Medical School, 1940
- LINCH, JOHN B.**, 660 Columbia Road, Dorchester  
Tufts College Medical School, 1929
- McCOLLUM, DONALD C.**, Free Hospital for Women, Brookline  
George Washington University School of Medicine, 1935
- MEZER, JACOB**, Free Hospital for Women, 245 Pond Avenue, Brookline  
Tufts College Medical School, 1936
- MILONE, ANTONIO P.**, 4354 Washington Street, Roslindale  
Middlesex University School of Medicine, 1934 Sponsor Charles J. E. Hickham, 12 Bay State Road, Boston
- PORTMAN, ABRAHAM**, 217 Washington Street, Islington, Westwood  
Middlesex University School of Medicine, 1935 Sponsor Boris E. Greenberg, 416 Marlboro Street, Boston
- REICHER, NORBERT B.**, Free Hospital for Women, Brookline  
Syracuse University College of Medicine, 1937
- RHINELANDER, FREDERIC W., 2ND**, 231 Perkins Street, Jamaica Plain  
Harvard Medical School, 1934
- RINKEL, MAX**, 439 Washington Street, Brookline  
University of Kiel, 1925 Sponsor Abraham Myerson, 475 Commonwealth Avenue, Boston
- ROSS, JOSEPH F.**, 11 Regent Circle, Brookline  
Harvard Medical School, 1936
- SINEONE, FIORINO A.**, Peter Bent Brigham Hospital, Boston (Roxbury)  
Harvard Medical School, 1934
- ZELLER, JOHN W.**, 154 Riverway, Boston (Roxbury)  
Harvard Medical School, 1933

Timothy F. P. Lyons, *Secretary*  
270 Commonwealth Avenue, Boston

## NORFOLK SOUTH DISTRICT

- CONLAN, WILLIAM P.**, 111 South Franklin Street, Holbrook  
Middlesex University School of Medicine, 1932 Sponsor Michael F. Barrett, 231 Main Street, Brockton
- NOBILI, CONRAD**, 14 Guild Street, Quincy  
Royal University of Rome Faculty of Medicine and Surgery, 1934 Sponsor Dr. Tonino V. Corsini, 23 School Street, Quincy

ORBACH, RUDI J., 279 Washington Street, Quincy.  
Royal University of Milan, 1934. Sponsor: William S. Altman, 32 Spear Street, Quincy.

SLOANE, WILLIAM C., 15 South Main Street, Randolph.  
Middlesex University School of Medicine, 1933. Sponsor: Jacob Applebaum, 808 Blue Hill Avenue, Dorchester.

SMITH, ROBERT M., 69 Elm Street, Cohasset.  
Harvard Medical School, 1938.

SWAN, DANIEL M., Norfolk County Hospital, South Braintree.  
University of Rochester School of Medicine, 1935.

Henry H. A. Blyth, *Secretary*  
24 Russell Park, Quincy

#### PLYMOUTH DISTRICT

GOLDFARB, SAMUEL, 19 West Central Avenue, Onset.  
College of Physicians and Surgeons, Boston, 1936.  
Sponsor: Raymond H. Baxter, 6 South Street, Marion.

LANDERS, THORNTON A., 20 Jenkins Avenue, Whitman.  
Middlesex University School of Medicine, 1917. Sponsor: Walter H. Pulsifer, 26 Park Avenue, Whitman.

Ralph C. McLeod, *Secretary*  
Goddard Hospital, Brockton

#### SUFFOLK DISTRICT

BARRY, THOMAS A., 58 Putnam Street, East Boston.  
Tufts College Medical School, 1936.

BELSKY, JOHN, 135 Chestnut Street, Chelsea.  
Boston University School of Medicine, 1934.

FIUMARA, NICHOLAS J., 75 Endicott Street, Boston.  
Boston University School of Medicine, 1939.

FREUND, ERNEST, 1163 Boylston Street, Boston.  
University of Prague, 1900. Sponsor: Walter Bauer, Massachusetts General Hospital, Boston.

GERBI, CLAUDIO, 234 Beacon Street, Boston.  
Royal University of Milan, 1931. Sponsor: Joseph H. Pratt, 30 Bennet Street, Boston.

GOGLIA, ALFRED A., 62 Bennington Street, East Boston.  
College of Physicians and Surgeons, Boston, 1936.  
Sponsor: Pasquale Costanza, 238 Maverick Street, East Boston.

KAPLAN, ISADORE, Soldiers' Home Hospital, Chelsea.  
Middlesex University School of Medicine, 1936. Sponsor: William H. Blanchard, Soldiers' Home, Chelsea.

KARP, I. ALBERT, 153 Shurtleff Street, Chelsea.  
Middlesex University School of Medicine, 1936. Sponsor: Arthur Berk, 270 Commonwealth Avenue, Boston.

LUONGO, ANGELO, 17 Vinal Street, Revere.  
Middlesex University School of Medicine, 1934. Sponsor: Themistocles V. Campagna, 195 Bay State Road, Boston.

REDLICH, FREDERICK C., Neurological Unit, Boston City Hospital, Boston.  
University of Vienna, 1935. Sponsor: H. Houston Merritt, Boston City Hospital, Boston.

SCHOENBACH, EMANUEL B., 119 Peterboro Street, Boston.  
Harvard Medical School, 1937.

Hollis L. Albright, *Secretary*  
412 Beacon Street, Boston

#### WORCESTER DISTRICT

BRAHM, LEO, Rutland.  
University of Berlin, 1924. Sponsor: Frank H. Washburn, Holden Clinic, Holden.

CROSBY, WALTER F., Maple Street, Sterling.  
Tufts College Medical School, 1939.

FUCHS, JACOB, 51 School Street, Milford.  
University of Vienna, 1923. Sponsor: Joseph Ashkins, 36 Pine Street, Milford.

GOLICKMAN, LOUIS, 99 Church Street, Whitinsville.  
Middlesex University School of Medicine, 1933. Sponsor: Harold V. Williams, 77 Cottage Street, Whitinsville.

HAIGHT, MEYER H., Main Street, West Warren.  
Middlesex University School of Medicine, 1934. Sponsor: John R. Fowler, 125 Main Street, Spencer.

HIGHT, DONALD, 7 Hancock Hill Drive, Worcester.  
Harvard Medical School, 1934.

KAUFMANN, PAUL E., 297 Main Street, Webster.  
University of Heidelberg, 1910. Sponsor: Leslie R. Bragg, 262 Main Street, Webster.

MULLOWNEY, JAMES P., City Hospital, Worcester.  
Loyola University School of Medicine, 1938.

NOSSIFF, GEORGE S., 241 Main Street, Milford.  
Middlesex University School of Medicine, 1933. Sponsor: Joseph Ashkins, 36 Pine Street, Milford.

ROTHSCHILD, ALFRED F., 167 Lincoln Street, Worcester.  
University of Munich, 1917. Sponsor: Joseph Muller, 36 Pleasant Street, Worcester.

SAVIGNAC, RAYMOND J., 35 Freeland Street, Worcester.  
University of Strasbourg, 1934. Sponsor: Alfred P. Lachance, 66 Parker Street, Gardner.

TELL, ABRAM B., 135 Chandler Street, Worcester.  
Kansas City University of Physicians and Surgeons, 1931. Sponsor: Edward Budnitz, 390 Main Street, Worcester.

WARD, ARTHUR D., Belmont Hospital, Worcester.  
Tufts College Medical School, 1938.

George C. Tully, *Secretary*  
34 Elm Street, Worcester

#### WORCESTER NORTH DISTRICT

HESS, FRANCIS, 38 Main Street, Gardner.  
University of Vienna, 1926. Sponsor: F. Richard Pierce, 14 Main Street, Gardner.

KULLN, ROBERT, 22 Prichard Street, Fitchburg.  
University of Munich, 1919. Sponsor: Samuel C. Golden, 150 Prichard Street, Fitchburg.

Edward A. Adams, *Secretary*  
40 Oliver Street, Fitchburg

#### DEATHS

POWERS — GEORGE H. POWERS, M.D., of Boston, died October 4. He was in his sixty-fifth year.

Born in San Francisco, Dr. Powers received his degree from the University of California Medical School in 1902. He was a fellow of the Massachusetts Medical Society and the American Medical Association, and was a member of the American Board of Otolaryngology and the American Otological Society.

He is survived by his widow and two daughters.

ROGERS — MARK H. ROGERS, M.D., of Boston, died October 5. He was in his sixty-fifth year.

Born in South Sudbury, Dr. Rogers graduated from Williams College in 1900 and received his degree from Harvard Medical School in 1904. He was professor of orthopedic surgery at Tufts College Medical School, chief

of the orthopedic service at the Beth Israel Hospital and orthopedic surgeon at the New England Deaconess Hospital. He was a fellow of the Massachusetts Medical Society, the American Medical Association and the American College of Surgeons.

His widow, a daughter, a son and two grandchildren survive him.

## BOOK REVIEWS

*Papers of Walter Hampton Frost, M.D. A contribution to epidemiological method.* Edited by Kenneth F. Maxcy, M.D. 8", cloth, 628 pp. New York: The Commonwealth Fund, 1941. \$3.00.

Frost, at the time of his death in 1938, was one of the leading epidemiologists in America. Brought up in the United States Public Health Service, a ground school for practically every important epidemiologist developed in this country, he was later chosen by William H. Welch to serve in the new School of Hygiene and Public Health established in 1919 at Johns Hopkins University. His previous work, particularly his accepted studies of acute antenatal poliomyelitis in Iowa, Ohio and New York, which were considered among the outstanding reports on the disease in this country, and his other studies on typhoid fever, sewage pollution and influenza had given him a worldwide reputation. After becoming established at Johns Hopkins, he showed great interest in tuberculosis, partly no doubt, because he suffered from this disease himself, and papers on this subject, in addition to the contributions on the principles of public health practice formed the bulk of his work during the latter years of his life. As these papers were widely scattered in medical periodicals, a committee of some of his friends and associates was formed in 1938, with Dr. K. F. Maxcy and others, to publish them in book form. The project had the sympathetic support of the Commonwealth Fund and a volume of over 600 pages is now available. The papers in general have been kept in their original form although most of the charts have been redrawn for uniformity. Dr. Maxcy has written a brief but stimulating introduction giving the chief facts about the life of Frost and an estimation of his scientific contributions and character. The frontispiece is an excellent reproduction of a photograph of Frost, and the whole volume is superbly printed. Rarely does one meet in medical publications such a satisfactory and fitting format. The frame, indeed complements the picture and the picture itself is of one of America's great epidemiologists. The world of medical literature has been enriched by the devotion of Dr. Maxcy to his predecessor and the farsightedness of the Commonwealth Fund in seeing that this book was published.

*Infantile Paralysis. Interior poliomyelitis.* By Philip Lewin, M.D. 8", cloth, 372 pp., with 165 illustrations. Philadelphia: W. B. Saunders Company, 1941. \$6.00.

This book is a careful review of all aspects of poliomyelitis with particular emphasis on orthopedic after care. Written by an orthopedic surgeon of note, this important aspect of the treatment of poliomyelitis receives adequate attention, with numerous illustrations of operative procedures. In the earlier chapters, however, on etiology, portals of entry, resistance and immunity, epidemiology and similar topics, as well as in those on examination and diagnosis, these points do not appear to be adequately covered. The ideas are sound, and the statements accurate in general although some may disagree with the

opinion expressed in the chapter on diagnosis. The book can nevertheless be highly recommended as an excellent brief account of a disease that is ever present and is a constant menace. This is a practical book of particular value to orthopedic surgeons and to the general practitioners who wish to understand the mechanics of orthopedic appliances and surgical procedures.

*Modern Drugs in General Practice.* By Ethel Browning, M.D., Ch.B. 8", cloth, 236 pp. Baltimore: Williams and Wilkins Company, 1940. \$3.00.

This is a list of drugs in common use, with a brief bibliography attached to each chapter. In most cases, the name of the drug, as supplied in Great Britain, is added, since the book emanates from British sources. It is a valuable, up-to-date listing of current pharmaceuticals, briefly presented, giving details about the drugs themselves, their clinical indications, dosage, toxic effects, the mode of action and the results of treatment. The book should prove to be of some value to American physicians, but other books of equal value, written from the American standpoint, are available.

## NOTICES

### ANNOUNCEMENT

DR. FRANK R. STENZEL announces the removal of his office from 1580 Beacon Street, to 1801 Beacon Street, Waban.

### SOUTH END MEDICAL CLUB

A meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, October 21, at 12 m. Dr. Donald E. Currier, chief of the Medical Division of the Massachusetts Selective Service System, will speak on "The Physician in National Defense."

Physicians are cordially invited to attend.

### JOHN T. BOTTOMLEY SOCIETY

The fourth annual clinical meeting of the John T. Bottomley Society will be held at the Carney Hospital on Wednesday, October 22, at 10:00 a.m. Luncheon will be served at 1:00 p.m. The annual dinner will be held at the Copley Plaza at 6:30 p.m.

#### PROGRAM

Erythroblastosis Fetalis Dr. William C. Moloney  
Recent Advances in the Treatment of the Menopause.  
Dr. John J. Thornton.  
The Management of the Acute Gall Bladder Dr. William J. Sullivan  
Common External Diseases of the Eye Dr. George R. Gagliardi  
Recent Advances in the Treatment of Skin Diseases  
Dr. John T. Foley

### NEW ENGLAND PATHOLOGICAL SOCIETY

A meeting of the New England Pathological Society will be held at the Boston Lying-in Hospital on Thursday, October 16, at 9 p.m.

#### PROGRAM

Morphologic Findings in Endometrial Biopsies from 100 Cases of Bleeding during the First Trimester of Pregnancy and from 34 Postabortal and Normal Puerperal Uteri. Dr. Robert N. Rutherford

Bilateral Cortical Necrosis of the Kidney: A report of 2 cases, with some observations on the pathogenesis and evolution of the renal lesion. Dr. Walter H. Sheldon.

The Relation of Ovarian Stromal Hyperplasia and Thecoma of the Ovary to Endometrial Carcinoma. Dr. Lent C. Johnson.

Observations on a Series of Early Normal and Abnormal Human Ova Obtained Prior to the First Missed Menstrual Period. Dr. A. T. Hertug.

Business meeting.

Collation.

## NEW ENGLAND SOCIETY OF PSYCHIATRY

The regular fall meeting of the New England Society of Psychiatry will be held at the Augusta State Hospital, Augusta, Maine, on Friday, October 17. Dr. Donald E. Currier, chief of the Medical Division, Massachusetts Selective Service System, will speak on "Medical and Psychiatric Features of the Selective Service Program."

## AMERICAN CONGRESS ON OBSTETRICS AND GYNECOLOGY

The second American Congress on Obstetrics and Gynecology will be held in St. Louis, Missouri, April 6 to 10, 1942. All the meetings and the commercial, educational and scientific exhibits will be held in the Public Auditorium.

The general plan for the program will be much the same as that of the first congress, which was held in Cleveland in 1939, with sectional meetings for the various groups (nurses, public-health officers, administrators, educators and physicians), general sessions for all members attending the congress and round-table discussions. The evening sessions will be open to the general public.

Admission to the congress will be by membership cards only, which may now be secured by the payment of a \$5.00 registration fee. All mail should be addressed to and further information may be obtained from the American Congress on Obstetrics and Gynecology, 650 Rush Street, Chicago.

## UNITED STATES CIVIL SERVICE EXAMINATION

### Maternal and Child-Health Specialists

Employment registers are to be established by the Civil Service Commission to fill maternal and child-health specialist positions in the Children's Bureau of the Department of Labor. Vacancies in similar positions in state agencies co-operating with the Children's Bureau may also be filled from these registers at the request of the states concerned. The examination announcement just issued by the Civil Service Commission to recruit persons for these positions allows the filing of applications until November 15.

There are three options in which persons may qualify: pediatrics, obstetrics and orthopedics. For each of these, employment lists will be established for administrative, research and clinical positions. The duties of the administrative positions include giving consultations and advisory service to state and other governmental agencies carrying out maternal and child-health programs. The research positions involve the planning or directing of studies in such fields as infant and maternal mortality, and child growth in relation to social, economic and other factors. Persons appointed to clinical positions will do clinical work in one of the options.

A written test will not be given for these positions. Competitors will be rated on their education, experience and corroborative evidence. Applicants must have graduated from a medical school of recognized standing and must have served a one-year internship. In addition, they must have had full-time postinternship clinical training, as well as other appropriate experience in the option selected and in the type of work in which they seek appointment.

Physicians who are interested in this opportunity are urged to seek further information about these positions, which pay from \$3200 to \$5600 a year. Further information and application forms may be obtained from the commission's representative at any first-class or second-class post office or from the central office in Washington, D. C.

## SOCIETY MEETINGS AND CONFERENCES

### CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, OCTOBER 12

#### MONDAY, OCTOBER 13

12 15-1 15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

#### TUESDAY, OCTOBER 14

\*9-10 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H Pratt Diagnostic Hospital.

12 15-1 15 p.m. Clinicoradiological conference. Peter Bent Brigham Hospital amphitheater.

8 15 p.m. Harvard Medical Society. Peter Bent Brigham Hospital amphitheater.

#### WEDNESDAY, OCTOBER 15

\*9-10 a.m. A Dental Pediatric Presentation. Dr. F. C. McDonald and Dr. Leonard Despres. Joseph H. Pratt Diagnostic Hospital.

\*12 m. Clinicopathological conference. Children's Hospital.

#### THURSDAY, OCTOBER 16

\*8 30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Children's Hospital.

\*9-10 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H Pratt Diagnostic Hospital.

8 p.m. New England Pathological Society. Boston Lying in Hospital.

#### FRIDAY, OCTOBER 17

\*9-10 a.m. Gastric Ulcer. Dr. Sara Jordan. Joseph H Pratt Diagnostic Hospital.

#### SATURDAY, OCTOBER 18

\*9-10 a.m. Presentation, with discussion, dispensary and district cases. Joseph H Pratt Diagnostic Hospital.

\*Open to the medical profession

OCTOBER 9-MAY 14. Pentucket Association of Physicians. Page 473, issue of September 18.

OCTOBER 11. American Social Hygiene Association. Page 559, issue of October 2.

OCTOBER 13-24. 1941 Graduate Fortnight of the New York Academy of Medicine. Page 834, issue of May 8.

OCTOBER 14-17. American Public Health Association. Page 579, issue of March 27.

OCTOBER 17. New England Society of Psychiatry. Notice above.

OCTOBER 19-23. American Academy of Ophthalmology and Otolaryngology. Page 350, issue of August 28.

OCTOBER 21. South End Medical Club. Page 599.

OCTOBER 22. John T. Bottomley Society. Page 599.

OCTOBER 29-30. New England Postgraduate Assembly. Pages 1111, issue of September 11.

OCTOBER 29-NOVEMBER 1. Association of Military Surgeons. Page 473, issue of September 18.

OCTOBER 30. Journal Club meeting, Boston Lying in Hospital, 8 p.m.

NOVEMBER 3-7. American College of Surgeons. Page 111, issue of July 31.

NOVEMBER 5-6. American Conference on Industrial Health. Page 473, issue of September 18.

JANUARY 3. American Board of Obstetrics and Gynecology. Page 473, issue of September 18.

JANUARY 10-11. Forum on Allergy. Page 392, issue of September 4.

APRIL 6-10. American Congress on Obstetrics and Gynecology. Notice above.

APRIL 20-24. American College of Physicians. Page 996, issue of June 5.

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## SOME USES AND ABUSES OF CHEMOTHERAPY IN PNEUMONIA\*

MANWELL FINLAND, MD,† OSIER L. PETERSON, MD,‡ AND  
ELIAS STRAUSS, MD,‡

BOSTON

THERE can now be little doubt concerning the value of the newer sulfonamide drugs in the therapy of pneumonia. Almost every physician has had some personal experience to demonstrate the effectiveness of sulfapyridine or sulfathiazole in this disease. There are, however, a number of important practical problems that require elucidation on the basis of recent accumulated experience. In this paper, we present our views on some of these problems.

### GENERAL CONSIDERATIONS

*Choice of sulfonamide drugs in the treatment of pneumonia.* The three compounds that have proved effective and have been used widely in the treatment of bacterial infections are sulfanilamide, sulfapyridine and sulfathiazole; a fourth drug, sulfadiazine, is now being evaluated. In the choice of a drug for use in the treatment of acute pulmonary infection, one thinks primarily of its effectiveness against the pneumococcus, which is the most frequent causative agent in pneumonia. However, when chemicals are equally effective against pneumococcus and other organisms that may cause pneumonia, other things being equal, the drug with the widest range of effectiveness is the one of choice. On the other hand, the drug of choice between compounds of similar efficacy is obviously the one offering the least likelihood of producing toxic effects.

In Table 1, we have summarized our evaluation of the toxicity of these four drugs, as well as of their relative effectiveness against the common causative agents of pneumonia. This is based

on our own experience and on the clinical and experimental data available in the literature. Obviously, sulfanilamide should not be used except in hemolytic streptococcus pneumonias, and then only when other drugs are not well tolerated. It is also apparent that until sulfadiazine becomes

TABLE 1 Summary of the Relative Toxicity and Efficacy of Four Sulfonamide Drugs in Infections with the Most Important Organisms Associated with Pneumonia

Drug	RELATIVE TOXICITY	RELATIVE EFFECTIVENESS IN CERTAIN INFECTIONS			
		Pneumo- coccus	Strepto- coccus femoralis	Staphy- lococcus aureus	Fried- lander's bacillus
Sulfanilamide	+++	+	++	0	0
Sulfapyridine	+++	+++	++	++	++
Sulfathiazole	++	+++	++	+++	++
Sulfadiazine	+	+++	+++	+++	++

available,§ the drug of choice in the treatment of pneumonia is sulfathiazole. Recent experience indicates that sulfadiazine has a wider range of effectiveness and is much less toxic than sulfathiazole, it is therefore our present choice for the treatment of pneumonia. The details of our studies with this drug are given elsewhere.<sup>1</sup>

*Route of administration.* Because the danger of renal complications is greater with parenteral chemotherapy, the oral route is always to be preferred. However, an initial intravenous dose of the sodium salt of the drug to be used is indicated in patients who are extremely ill, in those who are comatose, and in those with severe vomiting. Usually, a 5 gm. dose is given to the average adult, and may be followed by 2 or 3 gm. after about six hours. Although it is ordinarily recommended that this be given in distilled water as a 5 per cent solution, we prefer to give it intravenously as a 0.5 to 2 per cent solution in physiologic saline. For subsequent parenteral administration,

§Sulfadiazine has now been released for sale under the Federal Food Drugs and Cosmetic Act. Higher concentrations tend to precipitate out of solution from physiologic saline.

\*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1941.  
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§Research fellow in medicine, Harvard Medical School, assistant resident, Thorndike Memorial Laboratory, Boston City Hospital.

In all cases in which impairment of renal function is suspected, treatment should be undertaken with caution. Urines should be examined and the level of drug determined early in the course of treatment.

In the treatment of patients with pleural complications, it is important to differentiate sterile and infected pleural fluids. For this purpose, thoracentesis is performed, and the fluid obtained is examined for the number and character of the cells and for the presence of organisms in an ordinary stained preparation, and is also cultured. The absence of organisms in the stained smear and the presence of many mononuclear cells are presumptive evidence of a sterile effusion, but this should be verified by culture. In such cases, chemotherapy may safely be discontinued, since sterile fluids are usually absorbed spontaneously. In patients with purulent infected fluids, chemotherapy may be continued for a few days,

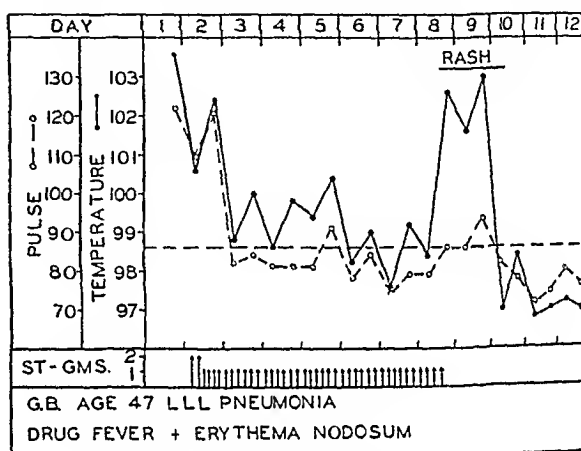


FIGURE 1. *Sulfathiazole Fever and Rash.*

In this and the subsequent figures, the following abbreviations are used:

♂ = male; ♀ = female.

SP = sulfapyridine; ST = sulfathiazole; SD = sulfadiazine; NaSD = sodium sulfadiazine.

L.L.L. = left lower lobe; R.L.L. = right lower lobe; and so forth.

C.F. = *pleural fluid*.

PN. I = *pneumococcus*, Type 1; PN. II = *pneumococcus*, Type 2; and so forth.

I.M. = *intramuscular*; I.V. = *intravenous*.

W.B.C. = leukocytes, thousands per cu.mm.; R.B.C. = erythrocytes, millions per cu.mm.

PMN = polymorphonuclear leukocytes.

N.P.N. = nonprotein nitrogen, mg. per 100 cc.

Blood culture: 0 = sterile; + = positive for pneumococcus; numbers represent colonies per cc. of blood; ∞ = innumerable.

but operation should be performed for drainage as soon as it is obvious that the infection is not yielding to treatment.

*Drug fever.* This is a frequent occurrence in patients under sulfonamide therapy and is sometimes difficult to differentiate from postpneumonic complications. Figure 1 shows the chart of a patient with drug fever during the course of chemotherapy. Such drug fever may or may not be

associated with rash and may be accompanied by chills. Frequently, the pulse rate remains relatively low, in spite of the elevation in temperature, and the symptoms of acute pulmonary infection do not recur. The leukocyte count may be somewhat elevated but is usually not very high during the early stages of drug fever. Cases of marked leukocytosis, however, have been noted. The diagnosis of drug fever is justified only when a characteristic rash is present or when the fever subsides within twelve to thirty-six hours after drug therapy is discontinued.

*Use of serum in pneumococcal pneumonias.* It is now generally agreed that sulfonamide therapy is to be preferred to serum therapy in all except the rare cases in which severe toxic reactions pre-

which adequate treatment with the drug fails to bring about the desired result in a reasonably short time, usually twenty-four to forty-eight hours. In some patients with infected purulent complications, adequate control of the infection may not take place until serotherapy is used, and large amounts of serum are often necessary under these conditions.

Obviously, it is impossible in retrospect to evaluate the relative role of each agent in cases in which both drugs and serum have been used. In the patients who survive, reasonable doubts may be raised about the part that the serum played in their recovery. In some of the fatal cases, it is equally reasonable to raise a question concerning what part the serum or the drug played in the

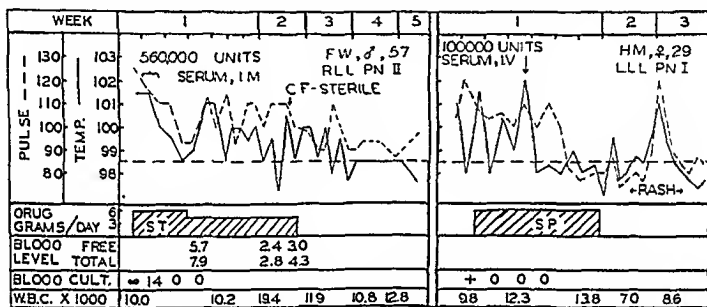


FIGURE 2. Two Patients in Whom Sulfonamide Therapy Was Supplemented by Antipneumococcus Serum.

clude the use of the drugs. Moreover, there is little doubt that the routine use of serum as an adjunct to chemotherapy is unwarranted, since it exposes the patient unnecessarily to the hazards of serotherapy. The differences in clinical response in the great majority of cases do not justify the added expense and effort. The availability of highly effective and relatively nontoxic drugs has now raised the question whether any patients receive sufficient additional benefit from serum to warrant its use as an adjunct to chemotherapy. Doubts concerning the additional value of serum are also based on serologic or statistical comparisons of cases treated with the sulfonamides alone and those in which such treatment is supplemented by serum. We have given long and serious consideration to this problem and believe that a definitive answer cannot be given at this time because of the great difficulty of obtaining conclusive data. Our experience leads us to consider additional serotherapy justified and necessary in individual cases. In general, these include some of the cases with the worst prognosis and those in

fatal outcome. This is particularly true when untoward reactions to either agent are encountered or when serum is given intravenously in the presence of cardiac or circulatory failure.

Figure 2 shows the charts of two patients who recovered after receiving serum in addition to chemotherapy. One patient (F. W.) was practically moribund at the time of admission to the hospital, and his blood was heavily invaded before the first dose of sulfathiazole was given. When serum therapy was started on the morning after admission, the patient had shown no signs of clinical improvement, although the bacteremia was partly but not completely controlled. The patient's condition was so poor that it was believed that the shock of intravenous serum therapy would be sufficient to turn the balance against him. Serum was therefore given intramuscularly, and no reactions resulted. The bacteremia was rapidly controlled, and a balance of antibodies was established within twelve hours after the first intramuscular dose. Although those who attended this patient agreed at the time that serum con-

tributed materially to the patient's survival, it cannot be stated with any degree of assurance that this patient would not have survived under sulfathiazole therapy alone.

It was believed that the other patient (H. M.) was not responding favorably after two days on full doses of sulfapyridine, whereas a dramatic response followed the administration of serum. In

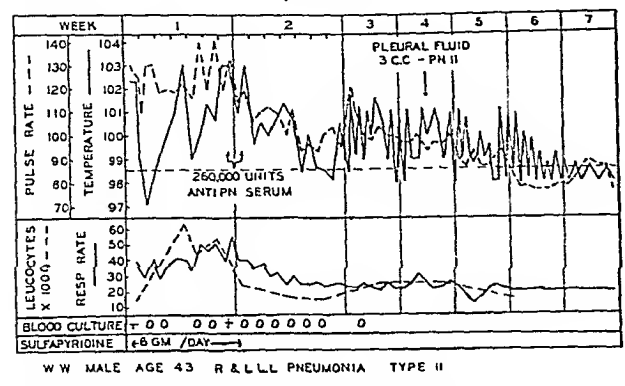


FIGURE 3. *Pneumonia with Bacteremia and an Infected Pleural Exudate, Treated with Sulfapyridine and Serum.*

this patient, the blood had already become bacteria free when the serum was given. One cannot tell with certainty what the course would have been had the serum not been given.

Cases in which failure to respond to chemotherapy was associated with resistance of the pneumococcus to the action of sulfonamide drugs have been described,<sup>4</sup> and it has been shown that in such cases a change from one effective drug to another cannot be expected to be of any help.<sup>4, 5</sup> Such cases do respond in the usual way to the administration of specific antipneumococcus serums. When serum treatment is delayed too long, however, it may prove ineffective.

Figure 3 shows the chart of a patient who illustrates another aspect of the use of serum. The blood was only temporarily rendered free of bacteria under chemotherapy. When serum was administered, the blood was rendered sterile and remained so in spite of the fact that chemotherapy was discontinued. In this patient, the presence of empyema was suspected, but only a small amount of infected fluid was obtained by thoracentesis. Recovery was complete at the time of discharge from the hospital, and surgical intervention was not required. This is another case in which, after serum had been given and the patient had recovered, the specific antibody probably contributed substantially to the recovery, but reasonable doubts may be raised.

The case of A. McL. (Fig. 4) illustrates still another aspect. At the beginning of treatment, this patient seemed to respond favorably; she then

had a relapse of symptoms, and the disease failed to respond to further chemotherapy. In this case, organisms could not be cultivated from the blood during the course of chemotherapy, but they were found in large numbers in the sputum. After the end of the second week of treatment, there developed a marked leukopenia, with complete absence of granulocytes in the circulating blood. Angina followed in spite of the fact that the drug therapy was discontinued. The patient responded to transfusions and pentnucleotide injections with a reappearance of granulocytes, but she had an invasion of the blood with Type 8 pneumococcus and died. It is not possible to say that the fatal outcome would have been averted if serum had been given during the first few days. Nevertheless, one cannot help believing that serum should have been given to this patient early during the relapse, making it possible to discontinue the drug and thus possibly to avert the fatal outcome.

The events in this case also serve to emphasize the value of making frequent blood counts in patients who are treated with sulfonamides for more than a week.

*Treatment of cases with leukopenia.* Because the sulfonamide drugs tend to produce leukopenia

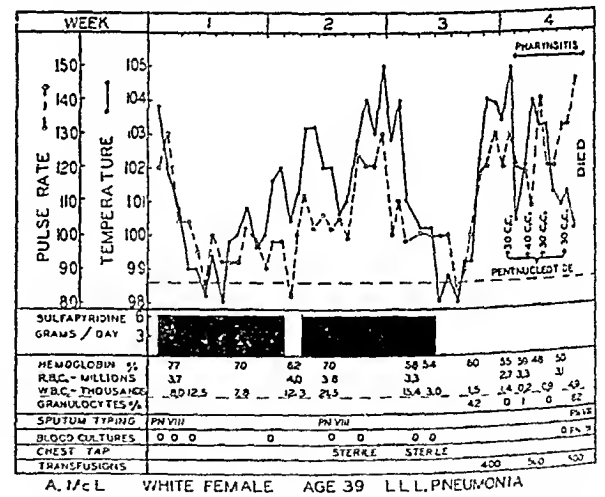


FIGURE 4. *Fatal Agranulocytosis in a Case of Pneumonia Treated with Sulfapyridine.*

and agranulocytosis on prolonged administration, there may be some hesitancy on the part of physicians to give the drugs to patients with low leukocyte counts. It should be emphasized that leukopenia in pneumonia is usually a manifestation of severe infection, and in such cases chemotherapy is definitely indicated. Of course, it must first be ascertained that the leukopenia is not the result of recent therapy with a sulfonamide drug. This is the only absolute contraindication to chemotherapy in the presence of severe infection. Accompanying the leukopenia, there is usually a bac-



teremia Because of the severity of the disease and the usually slow response in such cases, we believe that serum therapy should also be used

An example is shown in Figure 5 The patient was extremely ill on admission, and an initial dose of 4 gm of sulfadiazine was given by mouth A blood count made at the time of admission

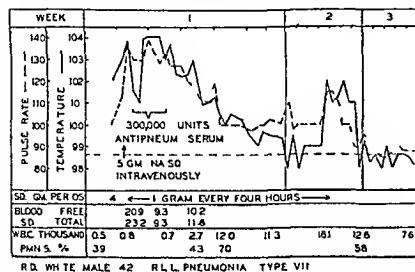


FIGURE 5 *Pneumonia and Severe Leukopenia Treated with Sulfadiazine and Serum*

Blood cultures made on admission and again before the first dose of serum were positive, the subsequent ones were sterile

showed that the patient had a white cell count of only 500, but there was a moderate proportion of granulocytes Chemotherapy was discontinued by the house physician on this account, and the results of pneumococcal typing were awaited However, drug therapy was considered to be indicated, and it was therefore resumed twelve hours later with an intravenous injection of 5 gm of the sodium salt of sulfadiazine, followed by regular oral doses Serum therapy was started shortly thereafter The blood culture was positive on admission and again before the first dose of serum was given The patient improved rapidly, but the temperature and pulse dropped only gradually during the next two days, after which the white cell count rose slowly to normal The role of serum therapy in the recovery is hard to evaluate, but one cannot help believing that it was an important factor

Blood cultures and bacteriologic studies of the sputum, including sputum typing, are of great help in prognosis and in the conduct of therapy It is essential to carry these out early if additional serum therapy is to be used successfully

#### SOME SPECIAL USES OF CHEMOTHERAPY IN ACUTE RESPIRATORY INFECTIONS

It is generally agreed that the present sulfonamide drugs are effective only in infections due to the common pathogenic bacteria and are indicated primarily for the cure of infections with such bacteria Nevertheless, it is general clinical experience

that many acute pulmonary infections respond favorably, although no organisms are recovered that are ordinarily considered etiologic in the disease or susceptible to the drugs

*Primary pneumonias of uncertain etiology* In common with many other observers, we have noted many cases of pneumonia that had all the clinical characteristics of typical lobar pneumonia, but cultures of the blood were sterile and examination of the sputum revealed no predominance of pneumococci, hemolytic streptococci, staphylococci or Friedlander's or influenza bacilli When the simple typing methods are resorted to, reports of "no pneumococci" are the rule The predominant organism in the sputum cultures is frequently *Streptococcus viridans* or a streptococcus producing only slight (alpha) hemolysis on blood agar Other organisms, such as *Micrococcus catarrhalis*, may also be found in moderate numbers, and staphylococci or influenza bacilli are sometimes found in small numbers The organisms found are usually nonpathogenic for mice, but occasionally one of the streptococcal strains may invade the blood of a mouse and give a fatal infection Many of these cases respond to chemotherapy in the same manner as typical pneumococcal pneumonias There are other cases with atypical pulmonary consolidation or with x-ray evidence of pulmonary involvement that is considerably more extensive than the physical signs indicate Some of these cases correspond to the ones that have recently been loosely called "virus pneumonias"<sup>6,7</sup> Such patients usually fail to respond to chemotherapy in adequate doses

In the patients who do respond, there is the likelihood that a pneumococcus was the responsible agent but was not recovered in the bacteriologic study The commonest cause for the failure to identify the pneumococcus is the failure to obtain proper sputum for the bacteriologic examination

From the practical point of view, it seems worth while to begin chemotherapy in all such cases and to discontinue drugs if after about forty-eight hours there is no definite evidence of improvement in the clinical course Further treatment subjects these patients to all the possible disadvantages of chemotherapy without offering much hope of beneficial effects

*Secondary pneumonias* We have been much impressed recently with the beneficial effects that may be obtained from chemotherapy in patients with acute pulmonary infections complicating severe and intractable asthma or a severe cardiac failure that does not respond to the usual therapy The administration of sulfonamides in such cases

is frequently accompanied by a drop in fever and pulse rate, and the underlying disease yields rapidly to proper treatment.

In Figure 6 are shown charts of 7 patients with asthma who had received all the usual therapy for this condition without effect. In each case, there were slight to moderate fever and leukocytosis. The physical signs varied. Some patients had only the usual signs of acute asthma, whereas others had moderate areas of consolidation, particularly in the base of the lungs. The first improvement of the

or in others who later prove to have pulmonary tuberculosis, there may occur acute exacerbations in the pulmonary symptoms, with dyspnea, fever, pleural pain, leukocytosis and the appearance of new areas of consolidation in the lungs. In such cases, these signs and symptoms are often due to superimposed bacterial infection, which yields promptly to chemotherapy, leaving the underlying tuberculosis unaffected. Possibly extension of the tuberculosis is averted or limited by such treatment. An example of a case of this sort is shown

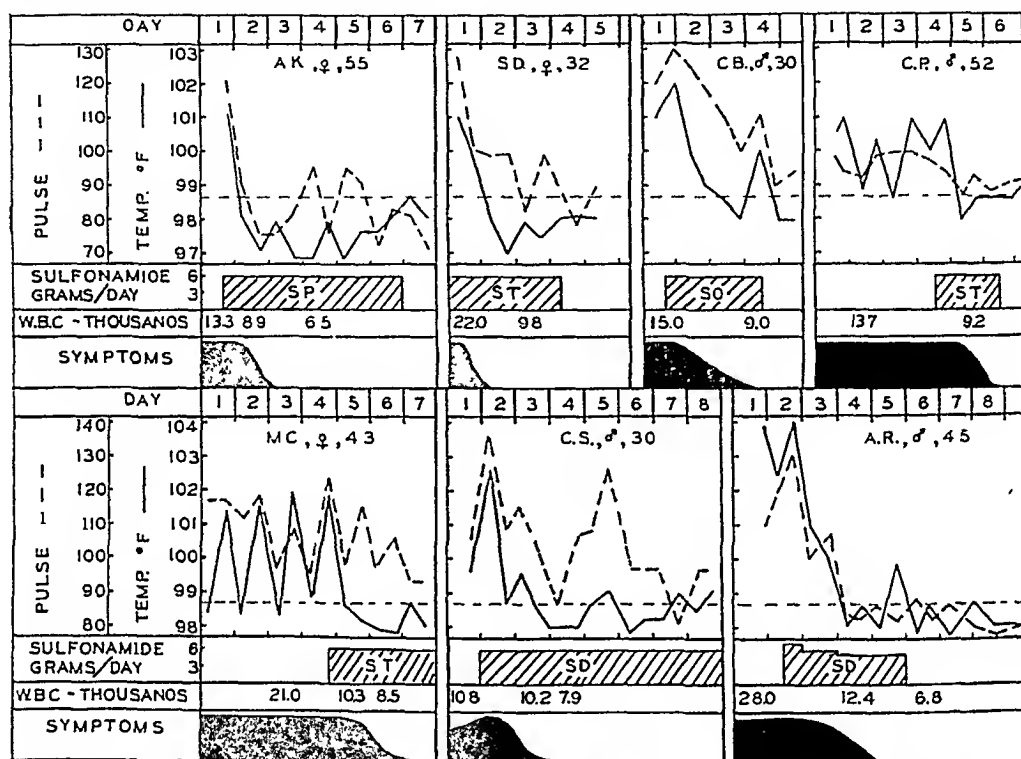


FIGURE 6. Seven Cases of Severe Acute Bronchial Asthma with Accompanying Acute Pulmonary Infections, Treated with Sulfonamides.

asthma occurred after the patients were given full doses of sulfonamide drugs, and coincided with the drop in fever. These are not cases that are ordinarily included among the pneumococcal pneumonias. In most cases, pneumococci were not recovered, the bacteriology of the sputum was similar to that of the cases just described, and blood cultures yielded no growth.

A group of 3 cases with congestive cardiac failure in which a dramatic response of the cardiac symptoms occurred only after chemotherapy is shown in Figure 7. There was fever in each case. The physical signs may have been attributable to pulmonary congestion or to pulmonary infection. In any event, these signs began to clear soon after sulfonamide therapy was started, and improvement in the symptoms of congestive failure followed rapidly.

In patients with known pulmonary tuberculosis

in Figure 8. The response in this patient was very similar to that usually seen in patients with acute pneumococcal pneumonia. The patient proved to have extensive pulmonary tuberculosis with a positive sputum, but the fever and symptoms subsided rapidly following treatment with sulfapyridine.

The course of events in the last case also serves to emphasize the advantage of following very carefully the fluid intake and output of patients receiving chemotherapy, regardless of the indications for the use of the drug. In this patient, there was a complete suppression of urine at the end of the second day of chemotherapy, after what seemed to be a good response of the acute infection. The patient was given large amounts of fluid parenterally and frequent injections of 50 per cent glucose intravenously without effect. Cystoscopy was performed after sixteen hours. Sulfapyridine crystals

were found in the bladder, in the left ureter and in both kidney pelvis; in fact, the left ureter was

the sulfonamide drug was effective in clearing up the acute pulmonary infection. The routine use

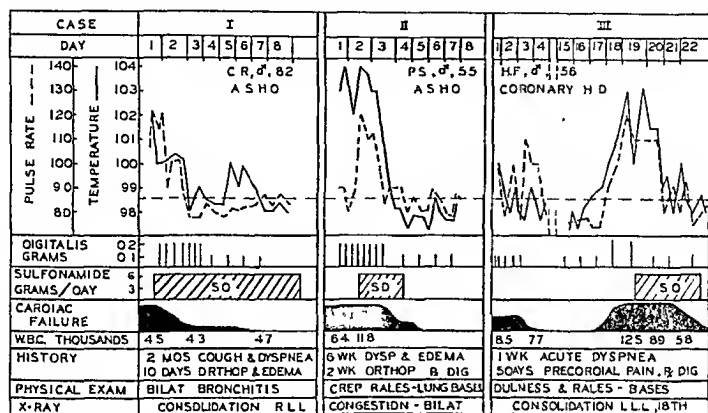


FIGURE 7. Three Cases of Congestive Cardiac Failure with Fever, Treated with Sulfonamides.

completely obstructed by clumps of these crystals. Ureteral catheters were inserted into the pelvis of the kidneys and kept in place for twenty-four

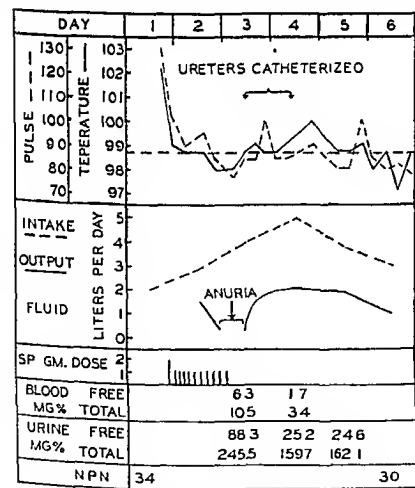
of sulfonamides in the treatment of asthma, cardiac failure or pulmonary tuberculosis is not recommended. In the absence of definite acute bacterial infection, no beneficial effects are to be anticipated, and the patient is subjected unnecessarily to the treatment. Furthermore, even in the presence of infection, the sulfonamides must be used with great caution to avoid untoward effects. In such cases, sulfonamide therapy should be discontinued in two or three days if the acute infection is not influenced, and should not be maintained for long periods in any event.

\* \* \* \*

In this brief presentation, it has been possible to consider only a few of the important problems concerning chemotherapy in pneumonia and to indicate some related situations in which the newer sulfonamides may be of great benefit.

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S G, WHITE MALE, 47 PUL. TUBERCULOSIS

FIGURE 8. An Acute Febrile Episode in a Case of Pulmonary Tuberculosis.

The anuria complicating sulfapyridine therapy was relieved by ureteral catheterization.

hours, following which the urinary excretion returned to normal.

It should be emphasized that in all these cases

## CARCINOMA OF 'THE ENDOMETRIUM'

## A Review with Results of Treatment Through 1935

GEORGE VAN S. SMITH, M.D.<sup>†</sup>

BROOKLINE, MASSACHUSETTS

IT HAS seemed to the members of the staff of the Free Hospital for Women that a clearer and broader perspective of our experiences with different forms of cancer is gained if we include in our periodic surveys the cases already reviewed in earlier studies, for longer follow-up gives new information about the survivors and, besides, patients formerly untraceable have in recent years been found in sufficient numbers to change appreciably the previous figures. Furthermore, evaluation of treatment can perhaps be better made by comparing earlier with later results in cases managed in the same clinic because of greater familiarity with the cases and a uniform method of reviewing them.

The present survey, which takes the place of previous publications on this subject from this hospital,<sup>1, 2</sup> the last of which carried five-year results through September, 1927, deals with 307 consecutive previously untreated<sup>‡</sup> cases of carcinoma of the endometrium seen from May 1, 1903, through December 31, 1935.<sup>§</sup> In every case, the diagnosis was made or confirmed by microscopic examination. For this writing, the pathology has been completely and critically reviewed, with the generous assistance of our pathologist, Dr. Arthur T. Hertig, and, through him as occasion demanded, of Drs. S. Burt Wolbach and Shields Warren.

## DATA CONCERNING PATIENTS

The youngest patient in this series at the time of treatment was thirty-three years of age, the oldest, eighty-five. Eighty-four per cent of the patients were over fifty, and 44 per cent over sixty. Forty-one per cent were nulligravidas. Eighty-five per cent had ceased menstruating.

*Relevant past history.* Three patients had had both ovaries removed fifteen, seventeen and thirty years respectively before admission. At the time

\*From the Free Hospital for Women.

<sup>†</sup>Assistant professor of gynecology, Harvard Medical School, visiting surgeon and director of the Fearing Research Laboratory, Free Hospital for Women.

<sup>‡</sup>During this same period, 15 patients who had had their primary therapy elsewhere received further treatment here. Eight died of recurrence less than five years after first treatment; 2 died of recurrence six to seven years after first treatment, 2 were well at eight and twelve years, having received prophylactic irradiation here; and 3 were well seven, nine and ten years after radium applied here for biopsied vaginal recurrence nineteen to thirty months after hysterectomy elsewhere.

<sup>§</sup>Omitted from consideration herein are 16 cases so diagnosed prior to May 1, 1903, because no pathological confirmation is available.

of castration, they were all under forty-three years of age. Five had had a radical mastectomy eight months to fourteen years previously. Curettage for abnormal bleeding had been performed on 13 patients five to thirty-three years before entry. A story of x-ray treatments for fibroids and flowing three years and six months to nine years before admission was given by 3. Five patients, 4 of them our own, had been treated successfully by radium (600 to 2400 mg. hr.) for flowing and endometrial hyperplasia, two to nine and a half years previously, and this diagnosis had recently been confirmed for all of them.

Of more immediate significance is the following past history. One patient had been taking ergot for six months for flowing that occurred fourteen years after the menopause. Another had had cysts of the ovaries removed for flowing at the age of fifty-eight, two years before hysterectomy here. A third had had a right salpingo-oöphorectomy for bleeding at the age of fifty-nine, six weeks before admission. Repeated x-ray treatments had been given for flowing to 3 patients for as long as three years without diagnostic curettage. Seventeen women gave a story of curettage one to twenty-four months before admission. Four had had curettage seven to thirty-six months previously, and the tissue had been reported not malignant. Despite persistent flowing, nothing further was done. Thus, about 9 per cent of the whole series had been mismanaged, with resultant delay of proper treatment, if their histories are entirely reliable. If careful examination under anesthesia with curettage of uterine cavity and endocervix and the taking of specimens for biopsy from suspicious areas of the cervix fail to reveal the cause of abnormal bleeding, dogged follow-up is demanded. Recurrence of bleeding thereafter requires immediate hysterectomy, unless a benign cause becomes clearly demonstrable.

*General physical examination.* As would be expected in a group of women for the most part past middle age, there were many in poor condition. Adequate physical examinations are recorded for 250 of the series, 56 per cent of whom had systolic blood pressures of 150 to 260; 28 per cent weighed 160 pounds or over, the heaviest pa-

patient weighing 276 pounds. Four per cent of the whole series had diabetes, 8 per cent had gall stones, proved by palpation at operation, and this figure is surely low, since the upper abdomen was not explored at every laparotomy and no gall bladder studies were performed on the majority of patients who did not come to abdominal operation. One patient had a duodenal ulcer, and only 1, a nulligravida, had procidentia. Arteriosclerosis was not often recorded, but it must have been rife. This assumption is borne out by the fact that the majority of later deaths not due to recurrent cancer were ascribed to vascular accidents and diabetes.

### TREATMENT

Tables 1, 2 and 3 summarize treatment and results. Removal of tubes and ovaries was included in all the hysterectomies. Thirteen patients were

were for other indications in younger women, 4 of whom had early, unsuspected endometrial carcinoma.

**Radiation** It was because of operative risk, obviously hopeless disease or both that radiation alone was employed in 36 cases. In the majority, only local palliation was expected. The "cures" by radiation alone were, apparently, the result of two purely chance occurrences, namely, that adequate radiation happened to reach all the growth and that the tumor happened to be radiosensitive. Before 1931, most patients treated by radium alone received single applications of 2400 mg hr. Three of the 5 surviving five years, however, had had 4800 mg hr. The capsules of the element in 0.5 mm of silver were placed, until 1926, in rubber tubing and, until 1931, in brass tubes of 0.5 or 1.0 mm thickness and inserted into the uterus. Between 1931 and 1935, inclusive, the radium was

TABLE 1 Summary of Treatment and Results Consecutive Cases, May 1, 1903, to 1925, Inclusive

TREATMENT	NO OF CASES	OPERATIVE DEATHS	STATS OF PATIENTS AT FIVE YEARS			STATS OF PATIENTS AT TEN YEARS			STATS OF PATIENTS AT FIFTEEN YEARS			
			UN-TRACE-ABLE	DEAD OF IN-UTERINE CUR-RENT DISEASE	ALIVE	UN-TRACE-ABLE	DEAD OF IN-UTERINE CUR-RENT DISEASE	ALIVE	UN-TRACE-ABLE	DEAD OF IN-UTERINE CUR-RENT DISEASE	ALIVE	
Untreated	6	1*	0	0	0							
Supravaginal hysterectomy	30	0	2	3	22 (63%)	1	2	3	16 (46%)	2	6	1 (0%)
Complete hysterectomy	60	6 (10%)	0	3	38 (63%)	2	2	4	29 (48%)	5	5	18 (30%)
Radium	17	0	1	0	2 (11%)	0	0	1	1 (8%)	0	1	0
Totals	113		3 (3%)		62 (54.8%)			8	46 (40.7%)		2	25 (22.1%)

\*Following exploratory laparotomy

†One patient also had primary carcinoma of the left ovary

‡In 1 patient the omentum was resected for a blood clot metastasis at the time of hysterectomy. 1 patient had metastases to the right tube and ovary at the time of hysterectomy. 1 patient had a carcinosarcoma of the endometrium. 1 patient also had in the myometrium a malignant tumor derived from an embryonic rest.

untreated because of hopelessly advanced disease, which was not determined in 9 until exploratory laparotomy. Three of these died postoperatively.

**Supravaginal hysterectomy** Obesity, cardiovascular disease, old age, fixation of the cervix and lower uterus deep in the pelvis by adhesions, shrunken supports or by scarring from inflammation and hopeless extension or metastasis, alone or combined, were the usual reasons why only supravaginal hysterectomy was performed on 69 patients of this series. A coring out of the cervix was included in 19, the first being done as early as 1906. Five of the supravaginal hysterectomies

applied in tubes of 1.0 mm of brass and 1.0 mm of lead for totals of 2200 to 4800 mg hr, these totals being reached in 8 cases by two treatments given two to four weeks apart. Before 1931, radiation was given to only 4 patients following operation, in total doses of 600 to 1800 r over a period of weeks. Since the group is so small and the value of the radiation as then administered so questionable, the cases are not considered separately.

**Preoperative radiation** Until 1931, radiation was not used as a primary treatment in conjunction with operation. Since radium had been of real

value in 5 of the cases unsuitable for surgery and in some cases with vaginal recurrences, a decision was made to employ it as a supplementary and prophylactic measure before or after hysterectomy. When used preoperatively, the capsules were placed in tandem in a tube of 1.0 mm. of brass and 1.0 mm. of lead from the top of the uterine

we are grateful for full co-operation. Portals of entry varied from 10 by 10 to 20 by 20 cm.; target distance was 50 cm.; filtration consisted of 0.5 mm. of copper and 1.0 mm. of aluminum; kilovoltage was about 200, and milliamperage 5 to 8. The great majority of individual treatments were of 400 r. Treatments were usually given daily for

TABLE 2. Summary of Treatment and Results, Consecutive Cases, 1926 to 1930, Inclusive.

TREATMENT	NO OF CASES	OPERATIVE DEATHS	STATUS OF PATIENTS AT FIVE YEARS			STATUS OF PATIENTS AT TEN YEARS			
			UN-TRACE-ABLE	DEAD OF INTER-CURRENT DISEASE	ALIVE	UN-TRACE-ABLE	DEAD OF INTER-CURRENT DISEASE	DEAD OF RECURRENCE	ALIVE
Untreated .	2		0	0	0				
Supravaginal hysterectomy	20	0	0	4	8 (40%)	0	0	2	6 (30%)
Complete hysterectomy	52	2 (4%)	2	3	35 (67%)	1	3	0	31* (60%)
Radium .	8	0	0	1	3 (38%)	0	1	0	2 (25%)
Totals	82		2 (2.4%)		46 (56.0%)	4		2	39 (47.5%)

\*One patient had metastasis to a benign pseudomucinous cystadenoma of the right ovary; 1 patient also had a highly malignant sarcoma in a fibro d

cavity to or through the external os for a total of 2400 to 3600 mg. hr. Four to seven weeks later, hysterectomy was performed.

The majority of patients receiving radium pre-operatively also received x-ray therapy, the rationale being, first, to affect possible metastases or

four days, usually through four portals, two anterior and two posterior. Four treatments totaling 1600 r were given immediately following radium application, and four more after hysterectomy. A few patients received only one series of 1600 r; the majority had a third series of 1600 r six to twelve

TABLE 3. Summary of Treatment and Results, Consecutive Cases, 1931 to 1935, Inclusive.

TREATMENT	NO. OF CASES	OPERATIVE DEATHS	STATUS OF PATIENTS AT FIVE YEARS		
			UN-TRACE-ABLE	DEAD OF INTER-CURRENT DISEASE	ALIVE
Untreated	5	2*	0	0	0
Supravaginal hysterectomy	5	0	0	1	2 (40%)
Supravaginal hysterectomy, radium, x radiation (treatments listed according to sequence)	7	0	0	0	7† (100%)
Radium supravaginal hysterectomy, x radiation	2	0	0	0	1 (50%)
Complete hysterectomy	15	2	0	1	9‡ (60%)
Complete hysterectomy, radium	3	0	0	0	2 (66%)
Complete hysterectomy, x radiation	11	0	0	1	9 (82%)
Complete hysterectomy, radium, x radiation	26	0	0	2	16 (62%)
Radium, complete hysterectomy	5	1	0	1	3 (60%)
Radium, complete hysterectomy, x radiation	17	1	0	2	9 (53%)
Radium	12	1†	1	0	3 (25%)
Radium, x radiation	4	0	0	1	2 (50%)
Totals	112		1		63 (56.2%)

\*Following exploratory laparotomy  
†Patient died of acute empyema of the gall bladder 21 days after the first radium treatment (weight 198 pounds, blood pressure 246/130).  
‡One patient also had primary carcinoma of the left ovary  
§One patient also had a primary carcinoma of the right ovary.

extensions beyond the sphere of radium's influence and, secondly, to reduce perhaps the chances of operative dissemination of the disease without causing in itself significant damage. During the period covered by this report, x-ray therapy was administered by Dr. John W. Meachen, to whom

months after the first for a total of 4800 r. During 1931 and the early months of 1932, some patients received as much as 5400 r in their first two series, the third bringing the total to 7000 r.

There have been, and still are, no definite indications to follow in the selection of cases for pre-

operative radiation. Some cases were so managed arbitrarily. With a few patients, however, this procedure allowed time to carry out regimens aimed at making them better operative risks. Moreover, when the uterus was considerably enlarged by tumor, it seemed that the shrinkage and drainage resulting from irradiation would facilitate operation. When there was cervical or vaginal involvement, preoperative radiation seemed clearly indicated.

*Postoperative radiation.* Between the second and tenth weeks of convalescence, a cylindrical "bomb," of 1.0 mm. of brass and 2.0 mm. of lead, containing 100 mg. of radium, was packed transversely across the vaginal vault, and allowed to remain for fifteen to thirty hours, the majority of doses being of 2000 or 2400 mg. hr. Postoperative x-radiation was started within eight weeks of operation, the technic, dosage and timing being as above described. Oftener than not, the first series of x-ray treatments preceded radium application.

Since 1935, combined x-ray and radium therapy has been employed practically routinely before or after operation and for those patients not considered eligible for operation. Radium dosages have been larger, at least 3000 mg. hr. preoperatively or at least 2400 mg. hr. postoperatively, and two applications two to eight weeks apart, totaling 4800 to 6000 mg. hr., for those not operated on. Since the fall of 1937, x-ray treatment, administered by Dr. Richard Dresser, has been given in a single consecutive series. Moreover, regardless of the sequence of therapy elected, an attempt has been made to complete all treatment within eight weeks.

#### OPERATIVE AND PATHOLOGICAL FINDINGS

*Extent of cancer of the endometrium.* In addition to the 13 patients whose disease was considered too extensive for treatment, 4 had vaginal metastases on admission, and 12 had adjacent or distant peritoneal spread. The disease was locally advanced, with fixation of the uterus in 10 cases; in 13 it had reached or grown through the uterine serosa. One patient without extensive local tumor had a presumed liver metastasis. Six cases had apparently localized ovarian metastasis, 1 of which also had a primary carcinoma of the opposite ovary.

*Associated malignant tumors.* One patient had an axillary recurrence of breast cancer on admission. Another underwent radical mastectomy here for carcinoma of the breast with axillary-node involvement, at which time intrauterine radium was applied as a preliminary to later hysterectomy. There was a concomitant inoperable squamous-

cell cancer of the cervix in 1 patient, and in 2, additional pathological study accidentally disclosed very early cancer of the cervix. One patient had four primary tumors—carcinomas of the ovary, cecum, ascending colon and endometrium. In all, 8 patients had a primary carcinoma of the ovary as well as primary endometrial neoplasm. Associated malignant neoplastic disease was present in 3 other patients: a rapidly growing fibrosarcoma of the cervix, a rapidly growing fibrosarcoma in a fibroid and a malignant embryonic rest tumor in the myometrium. Thus, 16 patients, or 5 per cent of the whole series, had more than one primary malignant tumor at the time of entry. Even though the data of this and the preceding paragraph are weighed optimistically, one is forced to conclude that at the very least 15 per cent of the whole series had an obviously poor prognosis when treatment was instituted. As shown in the charts, however, a poor outlook does not necessarily presage a fatal outcome, a fact that helps to maintain optimism in treating this disease.

*Other associated pathologic lesions.* Pelvic inflammation, chronic or with subacute exacerbation, was present in 45, or 17.4 per cent, of the 258 patients undergoing hysterectomy; fibroids were present in 79, or 30.6 per cent. Diffuse adenomyosis of the uterine wall was found in 5 cases, hemangioendothelioma of the broad ligament in 1 and a carcinoid of the appendix in 1. Benign conditions of the ovary were discovered as follows: pseudomucinous cystadenoma, 3; papillary serous cystadenoma, 3; dermoid, 2; fibroma, 2; endometrioma, 3; beginning papillary cystadenoma, 8; cystadenofibroma, 6; granulosa-cell tumor, 2; thecoma, 2; and bilateral thecoma, 1.

In examining the sections of the ovaries, I was impressed with the frequency of stromal-cell or thecal-cell activity, even to diffuse thecal-cell hyperplasia. Eighty-seven per cent (156 cases) of the available postmenopausal ovaries (180 cases) that were not involved by cancer or benign tumor had what was interpreted as slight to marked thecal-cell activity. One would expect such activity to indicate production of estrogenic hormone, and to be accompanied by corresponding endometrial proliferation, which, however, was not found to any striking degree in the available sections. Sections of endometrium had been prepared from 62 of the postmenopausal cases with apparent activity of the ovarian stroma and showed the following: atrophy, 14; slight proliferation, 35; definite proliferation, 11; and hyperplasia, 2. No correlation between the amount of stromal activity and the amount of endometrial activity was ap-

parent. Of course, the extent of the cancer made it impossible to obtain sections of the endometrium in a greater number of cases and in the above did not allow much choice of area to be sectioned. Moreover, in some cases it seemed that the proximity of the cancer itself gave the endometrium a little stimulation.

The relatively frequent association of endometrial cancer and granulosa-cell tumor appears to substantiate the opinion that continued estrogenic stimulation may carry endometrial hyperplasia on to cancer. The observation of a high percentage of thecal-cell activity in postmenopausal ovaries may perhaps be interpreted as indicating prolonged estrogenic stimulation of a degree insufficient to bring about significant endometrial proliferation, but it also involves the possibility of a reciprocal relation between ovary and endometrial cancer, namely, that the cancer itself may play a part in producing the ovarian change. It should be emphasized that thecal-cell hyperplasia is not in itself peculiar to the ovaries of elderly women with this type of cancer, being seen in various other conditions, but rather that there appears to be more hyperplasia associated with this disease.

Sections of the endometrium had been made from a total of 82 postmenopausal cases. In 62, the ovaries showed thecal-cell activity, as described above, in 12 they were atrophied, and in 8 no ovarian sections had been taken. The endometrial sections from all cases showed the following: atrophy, 22; slight proliferation, 45; definite proliferation, 13; and hyperplasia, 2.

Only 22 cases of the whole series had endometrial polyps, which were found in uteri with less advanced tumor. Many of the cancers themselves hung from the upper uterine cavity as polypoid masses, suggesting origination in a polyp. It is likely that this form of cancer starts in polyps oftener than can be demonstrated.

*Tumor pathology.* The malignant tumors were typed histologically as follows, the percentage of patients alive at five years being included in parentheses after each group: adenocarcinoma, 161 cases (62 per cent); adenocarcinoma with varying amounts of alveolar massing of undifferentiated cells, 115 cases (49 per cent); adenocarcinoma intermixed with more or less squamous-cell carcinoma, that is, adenoacanthoma, 25 cases (48 per cent); carcinosarcoma, 3 cases (33 per cent); squamous-cell carcinoma, 2 cases (100 per cent); and adenoacanthosarcoma, 1 (0 per cent). This typing is at best only roughly accurate concerning the first two groups, and depends in good part on the number of sections that happened to be taken from different portions

of the same tumor. For example, some sections from a tumor appeared to be purely adenomatous, whereas, others from the same tumor showed masses of undifferentiated cells or even areas of squamous-cell cancer. More sections from individual tumors might have changed the classification considerably.

Difficulties were also encountered in attempting to correlate the microscopic degree of malignancy with the duration of symptoms, the gross extent of the disease and the length of survival. It could not be shown that duration of symptoms or microscopic grade of malignancy bore any constant relation to the extent of the disease at the time of treatment or to the length of survival. In the first place, the degree of malignancy often appeared to vary in different areas of the same cancer. Secondly, duration of symptoms involved other factors besides the rate and extent of cancer growth. Some patients with advanced growth had had symptoms for only a short while, owing to cervical or vaginal atresia. Others, with protracted flowing, had highly active tumors still confined within the uterus, which apparently had formed a distensible but impervious barrier. Other cases, with tumors of low microscopical malignancy, had metastases without especially advanced local growth. A rare patient with confined tumor of not too high microscopical malignancy succumbed to exceedingly rapid recurrence without any change in the microscopical appearance of the tumor. Recurrences usually looked more active than the primary neoplasm. In others, whose cancers were of relatively high activity microscopically, the growth of recurrences was slow, sometimes to great size locally, death occurring as late as twelve years and eight months after operation.

Regardless of microscopical malignancy, it is difficult to understand why surgery alone should have cured a case with omental metastasis or with a surface metastasis to an ovary. In such cases, cancer cells must have been more widely disseminated and something must have prevented their "taking." The patients whose clinical courses failed to progress according to prognosis based on operative and pathological findings, for example, rapid recurrence of grossly confined, microscopically low-malignancy cancers or cures despite proved metastasis at the time of treatment, suggest that unknown constitutional factors either enhance or weaken resistance to endometrial cancer or cause the cancer itself to vary greatly in its malignancy, all regardless in general of the microscopical picture.



## RESULTS

One hundred and seventy one patients, or 55.7 per cent of the whole series of 307 cases and 58.1 per cent of the 294 treated cases, were alive at five years. Eighty five patients, 43.5 per cent of the 195 seen from 1903 to 1930, inclusive, and 45.4 per cent of the 187 who were treated, were alive at the ten-year interval. No attempt has been made to correct the survival figures because of the uncertainty regarding patients who died of intercurrent disease. Without autopsy they may not be considered free of recurrence. To simplify the figures, these and the untraceable patients are rated as dead of recurrence. Because 3 patients died of probable recurrence between twelve and thirteen years after operation, survival for at least thirteen years appears to be the criterion for absolute cure.

Of all the patients treated before 1931, 108 were alive at five years. Five became untraceable, 8 died of intercurrent disease, and 10 died of recurrence before the ten-year interval; 4 were living with recurrence at ten years. Thus, 75 per cent of those alive at five years were known to be alive and apparently free of disease at ten years.

As shown in the tables, the results for the years 1931 to 1935, inclusive, are no better than those of earlier years, despite the fact that 71 cases of this group, 66 per cent of the total treated, had had radium or x-radiation, or both, along with surgery. Forty-seven, 66 per cent, of these 71 patients were alive at five years. With surgery alone, however, practically as good five-year results were achieved. The failure to save more patients of this last group cannot be attributed to any change in operative technic and is probably explained as follows: 32 per cent had, at the time of treatment, extension of the disease, metastasis or another primary malignant tumor, as compared with 17 per cent of the cases listed in Table 1 and 22 per cent of those in Table 2. Although the extra manipulations and the delays attendant on pre-operative irradiation have been considered possible factors contributing to the unimproved results, it is more probable that the figures would have been poorer if irradiation had not been given. Furthermore, 6 of these 71 patients died quite definitely of intercurrent disease before five years. Although any advantage of supplementary irradiation cannot be demonstrated unequivocally, it is thought to have been of value. Of possible significance is the fact that only 4 of these, 5.6 per cent, had vaginal recurrence, as compared with 12, 6.3 per cent, of the 187 patients treated by operation only, and all these 4 patients had had advanced growth

locally when first treated. Two, 5.5 per cent, of the 36 treated only by irradiation had vaginal recurrence.

Evaluation of irradiation alone in this series may not be made, since it has not been employed in a sufficiently large number of unselected patients.

## OPERATIVE MORTALITY AND COMPLICATIONS

There were no operative deaths following supra-vaginal hysterectomy. Four patients developed incisional hernias, and 1 a vesicovaginal fistula, which was easily repaired.

Twelve, 6.3 per cent, of the 189 patients undergoing complete hysterectomy died postoperatively, 6 of pulmonary embolism, 4 of peritonitis and 2 of shock. Three patients developed incisional hernias, and 2 vesicovaginal fistulas, which were repaired satisfactorily.

No deaths or complications could be attributed to the use of radium alone. One death was assigned to the combination of radium and x-radiation:

Mrs E M I, at the time of complete hysterectomy on August 4, 1931, had metastatic cancer in the posterior vaginal fornix and the pouch of Douglas. Radium, 3000 mg hr, was applied to the vaginal vault 6 weeks later, following which 2700 r of 200-k.v. radiation was given. The same dose of x rays was administered 2 months later, and 2½ months following this, 2500 r were given, making a total of 7900 r within 6 months. Because of pelvic induration, thought at that time to be recurrent disease, and despite the fact that the patient felt quite well and was gaining weight, another radium treatment (2400 mg hr) was given. Increased pelvic induration and stricture of the rectum ensued, with disabling symptoms. Colostomy was performed elsewhere 2 years after operation, and death 8 months later was attributed to cancer of the rectum. From the course so long as followed in this clinic, it is probable that overirradiation caused death.

Severe proctitis without later disability occurred in 2 patients who received, following complete hysterectomy, 2400 mg hr. of radium, and 7000 r and 4800 r of x radiation, respectively. No fistulas have yet resulted from the irradiation given. There were only a few cases of transient irradiation cystitis.

*Retreatments.* Twenty four patients were treated by radiation for recurrence from a few months to nearly five years after first therapy. Eleven had vaginal, 1 a cervical, recurrence following operation only; 4 had vaginal recurrence after operation in addition to radiation, and there were 2 vaginal and 6 intrauterine recurrences after irradiation only. Only 1 remained permanently cured; 7 lived for six to nearly eleven years from first

treatment; 2 are alive, 1 with recurrence at eight years and six months, and 1 being well at nine years and three months. Recurrence after five years was in every case beyond any hope of palliation by local treatment.

*Associated malignant tumors.* It is known that 3 of the patients who had had a radical mastectomy before admission had mammary carcinoma. Sixteen more, as described above, had associated primary neoplasms at the time of treatment here. Two patients developed a new primary cancer following treatment of their endometrial cancer. In the first, a carcinoma of the ascending colon was removed two years and six months afterward. She is now well four years and two months after right colectomy. In the second, a primary carcinoma of the urinary bladder was found three years and eight months afterward, despite, or conceivably because of, the irradiation she had had previously. Further radiation and operation were of no avail, and she died fourteen months later. Thus, 21 patients of this series, or 6.8 per cent, had proved multiple neoplasms.

#### STATUS OF TREATMENT

From the results presented, it appears that complete hysterectomy, with bilateral salpingo-oophorectomy and removal of at least a small cuff of vagina, is still the primary desideratum in the treatment of cancer of the endometrium. The operation should include preliminary closure of the external os by suture to prevent possible spill of viable tumor, ligation of the tubal ostia for the same reason immediately on opening the abdominal cavity, and the avoidance so far as possible of direct trauma to the uterus during removal—for example, by applying clamps to the broad ligaments instead of grasping and thereby lacerating the fundus by instruments of traction, for fear of opening up channels of dissemination. These maneuvers have been practiced in the great majority of the complete hysterectomies herein summarized, along with a wide excision of the broad and infundibulopelvic ligaments. The fact that patients die of recurrence in spite of these precautions, even when the tumor is apparently confined within the uterus and the removed tissues show no microscopic metastases, suggests the possibility that the disease may be spread sometimes through uterine veins or lymphatics below the clamped portion of the broad ligaments by the motions necessitated during removal. This consideration intimates that clamping of the whole length of the parametria down to the vaginal vault as early as possible in the operation may be another worth-

while precautionary measure, for the accomplishment of which the vesicouterine flap and bladder would first have to be freed.

Improved results are being reported in small series of cases from the use of radium and x-rays alone. Perhaps if we treated a consecutive series with irradiation alone we could better our results. Of this we are skeptical, for of 24 cases (Table 3) receiving radium with or without x-rays on an average of a little over six weeks before operation, only 4 showed no evidence of the disease in the sections taken from the operative specimens. All had had 2400 to 3600 mg. hr. of radium, and 16 had received 1600 r of x-ray therapy as well. Admittedly, this is about half of what is here considered an adequate dose, but in recent years we have had the same experience with a number of cases in which full irradiation was used. These patients were at first thought unsuitable for operation. Five to fourteen months after full irradiation and general medical measures, a feeling of uncertainty led to operation, and in half the cases cancer was still present. We are not at all convinced that irradiation alone as now administered can supplant surgery in attacking this type of cancer.

Since, however, radium has been lifesaving in some patients with postoperative vaginal recurrence and, alone or with x-rays, has clearly prolonged life, we believe that, combined with x-radiation, it should be employed routinely, either before or after operation. When applied preoperatively, it should be so distributed as to affect the upper vagina as well as the whole length of the uterus.

#### SUMMARY AND CONCLUSIONS

A series of 307 consecutive, previously untreated, pathologically confirmed cases of carcinoma of the endometrium seen from May 1, 1903, through December 31, 1935, is reviewed with reference to past history, physical condition, treatment, operative and pathological findings, results, operative mortality, complications, retreatment for recurrence and associated malignant tumors. Previous irradiation for functional uterine bleeding in 8 cases did not inhibit the development of endometrial cancer. According to history, delay of proper treatment, which might have been prevented by the first physician consulted, occurred in 9 per cent of the series. Only 1 patient had procidentia. Five per cent of the series had more than 1 primary cancer at the time of treatment, and 6.8 per cent thus far have had proved multiple malignant neoplasms.

The observation has been made that a high per-

centage of postmenopausal ovaries in cases of this type of cancer show varying amounts of thecal cell hyperplasia, even to the extent of near thecoma formation, without, however, commensurate proliferation in the sections of endometrium that were available

No significant relation could be demonstrated between duration of symptoms, microscopic form or grade of malignancy, extent of cancer at the time of treatment and length of survival

Of all treated patients, 58.1 per cent were alive at five years. Of those treated before 1931, 45.4 per cent were alive at ten years. Of those living five years after treatment, 75 per cent were known to be alive and apparently free of cancer at ten years. Survival for at least thirteen years appears to be the criterion for absolute cure in this type of cancer.

One death was attributed to overirradiation. The combination of radium and x radiation produced a few temporary, nondisabling complications

Of 24 patients treated by irradiation for biopsied local recurrence less than five years after primary therapy, 12 were alive at five years, 2 survived for ten years and 1 was well at fifteen years

Although in this series irradiation alone has not been employed in a sufficient number of unselected cases to allow proper evaluation, from our experience with patients operated on following irradiation we believe that it cannot supplant surgery

Preoperative or postoperative application of radium and x radiation are considered valuable and probably necessary adjuncts to the best management of endometrial cancer, despite the failure to demonstrate in this series unequivocal improvement of results from their use

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## GLAUCOMA AND THE GENERAL PRACTITIONER\*

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GLAUCOMA causes about one third of all blindness in patients past middle life. A large percentage of blindness from this cause is preventable by recognized methods of therapy, provided the treatment is begun early. Because physicians in general medicine and surgery can play an important role in the control of glaucoma, this communication is presented.

In this discussion, I shall attempt to explain how glaucoma causes blindness, to review the diagnostic symptoms and signs, to describe briefly the treatment, and to point out how physicians may help in the prevention of blindness from this cause.

#### ETIOLOGY

Glaucoma means an intraocular pressure too high for the eye to withstand safely. Fluid is constantly passing into the eye through the ciliary processes and passing out again through Schlemm's canal. In the normal eye, the intake and outlet of fluid is so beautifully balanced that the intraocular pressure is maintained at a level of about

20 mm of mercury. In glaucoma, there is either an excessive inflow, or a blockage of the outflow, so that the pressure in the eye rises.

There are various theories concerning the etiology of glaucoma, but this problem is still unsolved. When the pressure in the eye is elevated for a long time, loss of vision results. If the pressure is extremely high, loss of vision is rapid. If the pressure is only moderately elevated, the loss of vision takes place more slowly. In either event, if the intraocular pressure is not controlled, the end result is total and permanent blindness.

Figure 1, which presents a series of visual fields, shows how vision is gradually lost from chronic glaucoma. In this disease, as the field charts indicate, the loss of vision is first in the periphery of the field. In many cases, central vision, or reading vision, is maintained until the disease is in the most advanced stage. Thus, the patient may not be aware of trouble until a large portion of the field of vision is lost.

Glaucoma may be primary or secondary. It is called secondary glaucoma when it is due to some obvious disease of the eye, such as iritis, uveitis, intraocular hemorrhage and certain forms of cataract, or to some operation on the eye, such as that

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for cataract. Although secondary glaucoma is sometimes the more difficult and intractable form, I need not discuss it here, for the patient is usually already in the hands of the ophthalmologist when this complication arises.

Primary glaucoma, which comes on without any obvious cause, is the type considered in this paper. It may be acute or chronic. These two forms are so different in their manifestations as

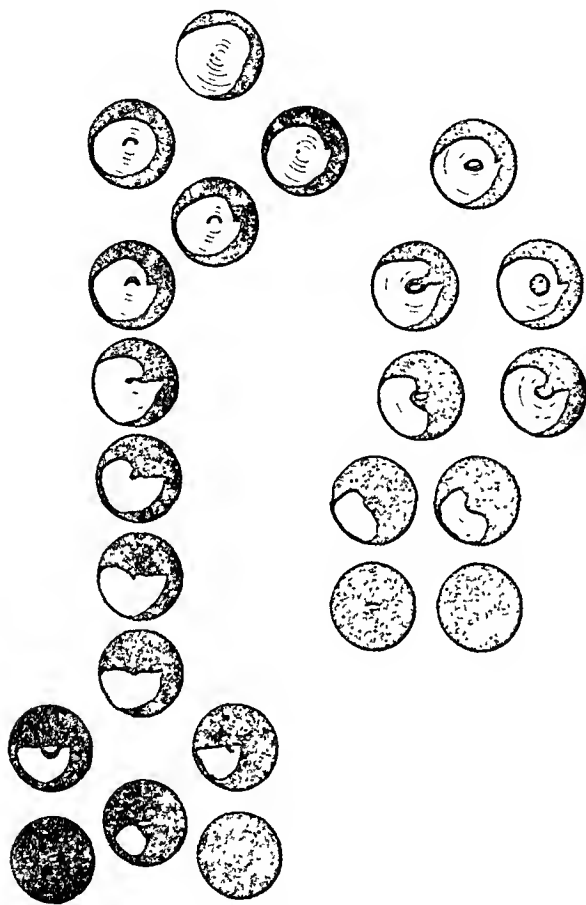


FIGURE 1. Chart Showing Progressive Impairment of the Visual Field in Untreated, or Inadequately Treated, Chronic Glaucoma.

*Most eyes take the course as shown by the field charts in the left column: here it can be seen that central vision is maintained until a very late stage in the disease. Rarely central vision is lost early, as shown in the field charts in the right column.*

almost to constitute two separate diseases. Figure 2 illustrates the difference between the two types. Thus, in acute glaucoma, the tension between attacks is not merely *almost* normal, but is, in fact, *absolutely normal*. Then comes a sudden rise in tension, to a greater or less degree, depending on the severity of the attack. In the chronic form, on the other hand, although the tension may vary greatly at various times, for practical purposes it can be said that the tension never

reaches the normal level. The eye is constantly subjected to various degrees of increased pressure, and this results in permanent structural changes in the eye, especially cupping of the optic disk, which causes a gradual loss of visual field.

#### SYMPTOMS AND SIGNS

In a typical case of acute glaucoma, there is often a history of mild prodromal attacks. These mild attacks may last from one to several hours; they are characterized by slight to moderate discomfort in the eye and blurred vision of varying degree, and the patient may see colored halos around lights. From such an attack, the patient may recover spontaneously, with the eye symptom free and as good as ever. Then comes the severe attack, from which there is no spontaneous recovery. With this, there is severe, often agonizing pain, rapid and profound loss of vision, and unusually uncontrollable nausea and vomiting. On examining the eye, one finds more or less congestion, a dull steamy appearance to the cornea, a shallow anterior chamber and a pupil that is nearly always partially dilated and fixed. On palpation, the eyeball feels much firmer than that of the unaffected eye.

Acute glaucoma must be differentiated from acute iritis. Severe pain, loss of vision and congestion of the eye may all be manifestations of acute iritis. In cases of iritis, the pain is usually less severe and comes on more gradually, and nausea and vomiting are absent. Aside from actual determination of the tension, the most reliable differential diagnostic point is the size of the pupil, which is larger than normal in glaucoma and smaller than normal in iritis. In acute glaucoma, the terrific pressure in the eye causes a temporary paralysis of the sphincter of the iris, and the pupil becomes larger than normal. In acute iritis, the engorgement and irritation of the inflamed iris cause spasm of the sphincter of the iris, and the pupil becomes smaller than normal.

In chronic simple glaucoma, the symptoms are not of much help in making the diagnosis. The patient may complain of mild pain in the eye, and of periods of blurry vision for hours or days. He may see colored halos around the lights at night. He may complain of seeing poorly in dim light, and of slowness to adapt when going into a darkened room. On the other hand, most patients have no complaints whatever until the disease has reached a relatively advanced stage.

Three signs are of chief diagnostic value: increased intraocular pressure, cupping of the optic disk and characteristic changes in the visual field.

To the well-trained ophthalmologist, the diag-

nosis of chronic glaucoma usually presents no difficulty. The intraocular pressure is accurately measured with a tonometer, the cupping of the disk is recognized by ophthalmoscopic examination, and the visual field defect is easily mapped out. There is no ocular disease with which chronic glaucoma need be confused.

### TREATMENT

An attack of acute glaucoma should be regarded as an emergency. If adequate treatment is begun within a few hours of the onset of the attack, vision is usually preserved. The later the treatment is begun, and the more inadequate it is, just so progressively worse becomes the prognosis. Forty

taken without delay, even though the operative risk to the eye in the presence of marked congestion and high tension is not inconsiderable and the operation is more difficult to perform. In some of these cases, classic iridectomy may relieve the condition only temporarily, if at all, and further operation may be required. In the late cases, all the efforts of the ophthalmologist may fail.

Aside from the difficulties in satisfactorily lowering the tension in the late cases, there is another even more important reason for instituting early treatment. Eyes vary greatly in their vulnerability to high tension. All ophthalmologists have seen eyes that have been subjected to a high

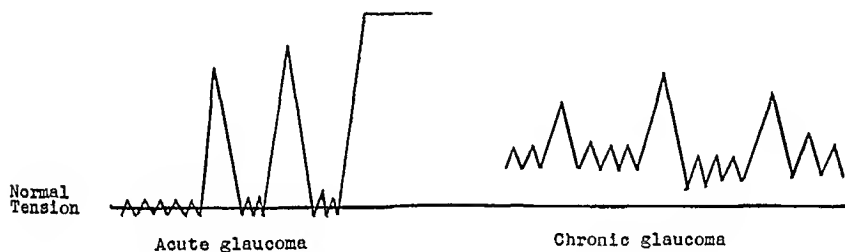


FIGURE 2 Diagram Indicating the Differences in Behavior of Intraocular Pressure in Acute and Chronic Glaucoma

*In acute glaucoma, the tension is always normal until the sudden rise in pressure during an attack. In chronic glaucoma, the tension may vary greatly, but is usually above normal.*

eight hours after the onset of the attack may be considered a sort of deadline, for if the beginning of proper treatment is delayed beyond this period, the prognosis is relatively poor.

The ideal treatment consists in lowering the tension to normal with pilocarpine or some other eye drop to constrict the pupil, and a few days later, when the eye is quiet, performing an iridectomy. If this is done, nine such eyes out of ten will remain completely and permanently cured. When the tension has been brought to normal with a miotic drug, both physician and patient may be reluctant to consider an operation. Except in very old patients, I believe that it is a serious mistake not to do an iridectomy, for without it, even with the continued use of drops, further acute attacks are almost certain to occur. It is not known exactly how the operation of iridectomy prevents the attacks in these cases, but the experience of generations has proved its effectiveness.

In many cases, especially if the attack has lasted more than forty-eight hours, it is impossible to lower the tension with pilocarpine or any other miotic. In these cases, operation must be under-

taken for only forty-eight hours and remain totally and permanently blind, in spite of complete relief of the tension. To be sure, most eyes can tolerate a high tension considerably longer than this and still recover part or all the vision if the tension is promptly lowered. However, there is no way of knowing which eyes can tolerate high tension and which cannot. One must act promptly, on the assumption that all eyes are vulnerable to high tension.

I have said that it is always advisable, if possible, to lower the tension with miotics before undertaking surgery. There are two points that deserve emphasis. The first concerns the type of drops used and the frequency of their administration. To prescribe 1 per cent pilocarpine three times a day for an eye in an acute attack of glaucoma is like throwing a straw to a drowning man, and about as effective. One should use 4 per cent pilocarpine or 1 per cent eserine, or one of the newer, more powerful miotics, such as Mecholyl and Prostigmine. The drops should be instilled every fifteen minutes for two or three hours, and at least every hour thereafter day and night until the tension is lowered to normal. The

second point in the use of drops is that they must not be relied on too long. A period of twelve hours may be considered an adequate trial. If after this time there is not a substantial lowering of the tension, surgery must be undertaken at once. In patients first seen several days after the onset of the attack, even twelve hours is too long to wait before operation is undertaken.

Chronic glaucoma constitutes no such emergency. Here there is plenty of time carefully to consider the pros and cons of various forms of treatment. The choice of treatment comprises the continued use of a miotic or operation, or both. There is no disease of the eye that calls for such sound clinical judgment concerning correct treatment, as chronic glaucoma does. It is not enough to make the diagnosis and prescribe eye drops to be used two or three times a day. One must be sure that the drops employed bring the tension to, and maintain it at, a sufficiently low level to prevent further damage to the eye. Only when a glaucomatous eye has been observed for some time can one surely say what is the normal tension for *this particular eye*. Some eyes tolerate a pressure up to 30 mm. of mercury without damage, whereas others will show progressive field loss with the pressure maintained at 20 to 25 mm.

In the management of chronic glaucoma, an accurate yardstick with which to measure the effectiveness of treatment is the study of the visual field. No patient suffering from chronic glaucoma is well treated unless periodic measurements of the visual field are made. If loss of visual field continues, treatment, whether it be medical or surgical, has been inadequate. In such cases, whatever the level of the tension, it is too high for this particular eye. The treatment must be revised, or total blindness in the eye will result.

I shall not attempt to discuss the indications for operation in chronic glaucoma. Suffice it to say that the younger the patient the stronger the indication for operation. I believe that most patients under the age of sixty who are in good health and have a normal life expectancy should have operation. Even the most faithful use of drops often fails to hold the disease in check over a period of years. However, each case must be decided on its own merits, and no fixed rules can be laid down. It is not an easy thing for the ophthalmologist to advise surgery on a symptom-free, normally seeing eye. An operation successful in lowering the intraocular pressure may not only fail to improve the vision but may actually lessen it. There is no dramatic restoration of vision here as in the extraction of a cataract. Yet,

if one undertakes to treat the disease at all, one must not hesitate to treat it properly.

#### PREVENTION OF BLINDNESS

General practitioners are often the first to see the patient with acute glaucoma. In every case of severe nausea and vomiting, especially when accompanied by pain in the eye or headache, they should consider this possibility. The patient may be so sick as to forget about the eye and complain only of nausea, vomiting and general prostration. In the early stages, congestion of the eye may be very slight, and may easily escape attention if it is not looked for especially. If there is the slightest doubt whether the case is one of acute iritis or acute glaucoma, it is best not to give any treatment at all. In an attack of acute glaucoma, one drop of atropine may mean the ruin of an eye, for the effect of the atropine is not only deleterious but cannot be overcome by miotics. When the diagnosis has been made, it is the attending physician's responsibility to see that there is no delay in the institution of treatment. The patient may be prostrated by the disease, but he is never too sick to be moved to a place where proper treatment can be carried out. He will never get better until the tension is lowered.

In chronic glaucoma, the physician is not often called on to make the diagnosis. Yet many physicians discover glaucomatous cupping of the disk in routine ophthalmoscopic examination. When the patient has a visual complaint, he should be referred to a physician qualified to diagnose and treat any disease of the eye. The patient should not be permitted to disregard ocular pain, blurred vision, seeing colored rings around lights, poor vision in dim light and slow adaptation to darkness. When a patient who complains of loss of vision is referred to the ophthalmologist, the physician is entitled to an adequate explanation of this symptom. When the diagnosis of chronic glaucoma is made, one can be of considerable help to the ophthalmologist by urging that the patient faithfully carry out the treatment recommended. The patient should be urged to report for the periodic check-ups that are so important in the treatment of this disease. The physician can help more than a little in getting the patient adjusted to the situation: his advice is invaluable in helping the patient to avoid the stresses and strains of life, particularly the emotional strains, which have such a distinctly unfavorable influence on the disease. I may say in passing that glaucoma bears no known relation to any constitutional disease.

Patients past middle life should have a thorough

check up of their eyes at least once every two or three years. Most cases of chronic glaucoma are discovered in just such routine examinations. A check up once a year in older people is not too frequent. It makes no difference if they are known to have partial loss of sight from retinal disease or incipient cataract. Glaucoma can coexist with any disease of the eye. The most tragic situation has many times arisen in cases when both incipient cataract and glaucoma are present. The patient may be advised of the presence of the cataract and may watch his vision slowly fail, expecting when he is entirely blind to have his vision restored by cataract extraction. One often has to tell such patients that, true enough, a partial or complete cataract is present, but that all vision has been irretrievably lost from glaucoma. Vision lost from chronic glaucoma can never be restored. One should therefore do everything possible to prevent blindness from this disease.

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#### DISCUSSION

DR. CHARLES F. NUTTER (Nashua). There is much to learn about glaucoma. Dr. Chandler's exposition of this subject was very clear, but perhaps some of the things he said are not clear to those who are not particularly interested in the disease. Great stress has been properly laid on the increased hardness of the eye. There is pressure on the nerve, which is the weak part of the wall, of course.

Although some ophthalmologists may disagree with me, I have seen cases in which the tension was reduced to

normal, but in which progressive blindness occurred, so that later on, the eye was of no use. In those cases, one may be able to find some reason for it. But I believe that some element is present with which we are not really familiar.

Dr. Chandler spoke of the danger of one dose of atropine. I remember a case in which a physician was called to see a patient who had a bilious colic. The pain was not referred to the head; it was underneath the right shoulder blade, extending down into the region of the gall bladder, with every symptom of the passing of gallstones. The patient was given large amounts of morphine and atropine. The next morning, he was totally blind, and remained so, despite all treatment. If you want to give morphine, all right, but leave the atropine out.

One other thing that is very important is the early recognition of glaucoma. I believe that many cases are frequently overlooked, even by ophthalmologists. Consider the large percentage of patients who are wearing glasses, cases of blurring; some of them are at least temporarily blind, and they keep going back to the optometrists or someone who is not legally qualified to make diagnoses. Consequently, many cases of glaucoma get ahead of us. I think that when receiving a prescription for glasses, all patients should be seen by someone who is able to understand and recognize the symptoms of a case of chronic glaucoma.

DR. CHANDLER (closing). It is true, as Dr. Nutter said that we, as ophthalmologists, have a long way to go before we know the answer to glaucoma. Yet the fact is that although we fail in a certain number of cases, there is no excuse for the conception in the mind of the average layman that glaucoma means blindness. I think it is fair to say that in the vast majority of cases, if the diagnosis is made reasonably early, and if the condition is properly treated, the patient with this disease may have useful vision so long as he lives.

## MEDICAL PROGRESS

### SURGICAL CARE AND OPERATIVE TECHNIC\*

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THE current general surgical literature continues to attest to the diversity of modern surgical interests. Much attention is given to such major topics as nutrition, sulfonamide therapy of infections and wound healing. Increased interest in shock and problems of trauma is seen as an inevitable concomitant of war; this was also true in World War I.

#### NUTRITION

Continued advance in the understanding of the relation between nutritional deficiencies and post-operative complications is evident. As the pre-operative condition of the patient is studied more generally and with improved methods, two facts stand out—that nutritional deficiencies are frequently multiple, and that they are often present in latent or subclinical form.<sup>1</sup> Thus, it may happen that unsuspected borderline vitamin or protein deficiency is intensified by the stress of the surgical ordeal and the postoperative period of starvation, with resultant grave complications. The postoperative bleeding of prothrombin deficiency, delayed wound healing or wound dehiscence, malfunction of a gastroenterostomy stoma, postoperative psychosis and liver failure may be taken as illustrative examples.

The importance of the plasma proteins in surgical problems is discussed by Ravdin,<sup>2</sup> who states that it is not only the measurable concentration of the plasma protein that is significant, but also the amount of the reserve or storage protein. Madden and Whipple<sup>3</sup> present the concept of dynamic equilibrium between the body protein stored as a reserve against adversity and the nitrogenous elements in active metabolism. If the exogenous supply of protein is suddenly cut off, the immediate consequences depend on the state of the available reserves. These authors believe that new plasma protein probably flows largely from the liver, although some globulins may be formed elsewhere.

Hartzell, Winfield and Irvin<sup>4</sup> describe their

\*All articles in this series will be published in book form: the current volume is *Medical Progress: Annual, 1940* (Springfield, Illinois: Charles C Thomas Company, 1941. \$4.00).

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findings in a study of biochemical changes in the plasma of 20 patients at the time of dehiscence of laparotomy wounds. In 14 with dehiscence of clean wounds, the average plasma vitamin C concentration was 0.36 mg. and the serum-protein concentration 5.83 gm. per 100 cc., and the albumin-globulin ratio 1.25; in 6 patients with dehiscence of infected wounds, the respective values were 0.38 mg., 5.84 gm. and 1.30. Average normal values in a group of 20 medical students were found to be 0.96 mg. per 100 cc. for plasma vitamin C and 7.19 gm. per 100 cc. for serum-protein concentration. The authors emphasize the value of correcting deficiency of vitamin C and plasma protein before operation.

In the treatment of hypoproteinemia in surgical patients, Casten and Bodenheimer<sup>5</sup> report that in their experience the administration of massive transfusions of plasma provokes the greatest and most sustained rise in serum proteins. They point out that since the liver holds the key position in maintaining normal stores of plasma protein, all the measures known to favor liver function should be taken, including the administration of carbohydrate, protein and vitamins in adequate amounts. Elman<sup>6</sup> discusses the usefulness of intravenous aminoacid infusions in the correction of protein deficiency. The title of his paper, "Parenteral Replacement of Protein with Amino-Acids of Hydrolyzed Casein," is not free from Hibernicism, since aminoacids cannot substitute for body protein directly, but become protein only through synthetic cellular activity. The usefulness of aminoacid mixtures obtained by enzymatic hydrolysis of casein in the maintenance of nitrogen balance when administered intravenously is receiving confirmation in a number of clinics. In my experience, such therapy is effective even in the presence of severe liver damage.

The occurrence of prothrombin deficiency as a complication of perforative appendicitis and manifested by massive hemorrhages from the operative wound has been reported.<sup>7</sup> It is recommended that in the management of peritoneal sepsis, particularly if it is of gastrointestinal origin, the plasma prothrombin value be determined at frequent intervals and vitamin K be given parenterally if needed. Hypoprothrombinemic bleeding



may take place in these cases even in the absence of signs of toxic hepatitis and hepatic impairment.

### HEPARIN

Clinical experience is accumulating by which the proper place of this anticoagulant can be estimated. Murray<sup>8</sup> lists the indications for heparinization as follows: arterial suture, excision or repair of arteriovenous fistula, venous grafting, embolectomy and mesenteric thrombosis. In addition, he reports that the prolonged morbidity, discomfort and disability following thrombophlebitis and phlebothrombosis can be reduced by the administration of heparin for four to eight days, as shown in experiences with over 125 patients. He has encountered no cases of pulmonary embolism attributable to the use of heparin, and he rightly points out that heparin has no effect on the established clot. In considering the disadvantages of heparinization, to the drawback Murray mentions—the necessity for immobilizing the patient while he is receiving a constant infusion—may be added the expense, the difficulty in maintaining even and moderate delay in clotting, and the need for frequent determinations of clotting time. Possible interference with inflammatory fixation of bacteria is also to be kept in mind.

Some of the disadvantages of heparin in the maintenance of delayed coagulability in patients may be obviated if further clinical trial supports preliminary observations on the use of a coumarin derivative isolated by Link et al.,<sup>9</sup> of the University of Wisconsin. This substance has recently been identified as the chemical element responsible for the impairment of clotting seen in cattle suffering from the effects of eating spoiled sweet clover. When taken by mouth, the drug inhibits clotting over a period of several days, apparently without other ill effects.

Lehman and Boys<sup>10</sup> report interesting experimental results in the use of heparin in preventing peritoneal adhesions. Their work has been done entirely on animals and does not as yet permit clinical application. They summarize their observations as follows: intraperitoneal heparinization in three daily doses of at least 1000 units largely prevents the re-formation of divided peritoneal adhesions in the dog; hemorrhage following the intraperitoneal administration of heparin is not a danger if hemostasis is complete before the heparin is administered; and contamination of the peritoneum does not appear to be a contraindication to the intraperitoneal use of heparin.

### OPERATING-ROOM INFECTIONS

Continued interest is shown in reducing infection of clean surgical wounds as near as possible

to the ideal zero. In a study<sup>11</sup> of the condition of the wound after 606 clean operations, infection of some degree was found in 3.81 per cent, whereas in 1.59 per cent infection was sufficiently severe to prolong the patient's stay in the hospital or endanger life. These figures are probably indicative of the incidence in the average well-run surgical service. Since efforts at further improvement in surgical technic must be directed at the occasional poor result, the challenge here is evident. Hart<sup>12</sup> reports on further experiences with the method he has devised for sterilization of the air in the operating room by bactericidal radiation. He has encountered no untoward results beyond an occasional erythema in members of the operating team who neglected the proper covering. Hart considers the technic to be practical, safe and effective, and states that a significant reduction in wound infection has resulted from its use in his clinic. It should be noted, however, that the method has yet to win approval elsewhere. Rice, Weed and Raidt<sup>13</sup> point out that satisfactory investigation of the bacterial content of the operating-room air can be done only with the air centrifuge of Wells, for the Petri dish method gives misleading results.

Two excellent studies have been reported during the past year on the effectiveness of surgical masking. Hirshfeld and Laube<sup>14</sup> have devised a method for testing masks under conditions of actual use, involving measurements with the Wells air centrifuge. Their most significant conclusion is to the effect that masking of the operating team would be unnecessary if no one talked. They find that the direct spray contamination of talking is greatly reduced when a mask is worn but is still higher than that of quiet breathing without a mask. As tested by their method, the usual four-ply or six-ply gauze mask is grossly inadequate, especially after it has been worn for a while. Rooks, Cralley and Barnes<sup>15</sup> have investigated the value of various types of hospital masks with respect to bacterial filtering efficiency and resistance to air flow. They point out that a completely impervious mask has no value, merely serving as a deflector of the organisms, whereas a highly porous, and hence comfortable, material may have poor filtering power. They find that repeated laundering of masks improves filtering efficiency without proportionate increase in resistance to the breath.

### SUTURE MATERIAL AND WOUND HEALING

Judging from the number of reports in the current literature on the use of other suture materials, one would suppose that surgeons are highly dissatisfied with catgut and silk. No less than nine

papers are at hand dealing with the subject. Alloy steel wire has acquired a considerable measure of esteem since its introduction by Babcock in 1932. Jones, Newell and Brubaker<sup>16</sup> state that the substitution of steel wire for catgut has resulted in lowering of the incidence of wound disruption following operations on the biliary tree from 11.0 to 1.2 per cent, whereas the incidence of infection in abdominal wounds after combined abdominoperineal resection and midline colostomy has fallen from 27.5 to 0.85 per cent. They use a series of buried figure-of-eight wire sutures for the peritoneum and rectus sheath, and dispense with stay sutures. In a study by Preston<sup>17</sup> of the tensile strength of skin wounds in white rats sutured with annealed stainless steel wire and with other suture material, the wounds closed with wire had greater strength and showed less local reaction. This author points out that the surgeons' gloves may be torn by the wire ends and that injury to the surgeons' hands in an infected field may occur. Careful technic is essential in using the wire.

Holman and Eckel<sup>18</sup> advocate the use of 20-gauge silver-wire stay sutures in laparotomy wounds. All layers are included, and the separate layers are united with No. 0 chromic catgut. The wire through-and-through sutures are removed in fourteen to sixteen days if no infection is present.

Further experience with the use of cotton thread for suture material tends to confirm original impressions concerning the validity of the technic. Localio and Hinton,<sup>19</sup> on the basis of personal observations, discuss the manner of using cotton thread and the most satisfactory grades and brands. They recommend that cotton thread be sterilized by boiling from ten to twenty minutes and used while wet, for its tensile strength diminishes on drying.

Enthusiastic reports are at hand on the experimental and clinical results of the use of synthetic plastic fiber as buried sutures. According to Aries,<sup>20</sup> Nylon sutures are well tolerated by tendons and nerves, and do not evoke a leukocytic or even lymphocytic response. In infected wounds, Nylon acts much the same as silk in holding the tissues securely and remaining unchanged, and the author concludes that Nylon has all the good qualities of silk and in addition is stronger and less irritating. It may be boiled several times without losing its original strength. Aries recommends a multifilament rather than a monolithic Nylon thread, for although the former evokes slightly more local reaction, it is far easier to handle and the knots are safer and less bulky. Bellas,<sup>21</sup> after using a synthetic plastic-suture ma-

terial in over 600 wounds, is similarly enthusiastic. In work on guinea pigs and dogs, he finds that remarkably little local reaction is produced by this suture material.

In a careful and well-planned study of factors influencing the tensile strength of healing skin wounds in animals, Botsford<sup>22</sup> finds extracts of spleen and other tissues of no value in accelerating healing. He describes experiments showing the value of secondary suture of wounds, in support of accepted clinical practice. The superiority of silk over catgut is apparent in these investigations, according to the author. In establishing the normal curve of tensile strength of healing skin wounds in guinea pigs and dogs, Botsford notes considerable variation in the ability to heal among supposedly healthy animals and in the individual animal with multiple wounds; these matters should be kept in mind in any consideration of the question of wound healing.

#### SURGICAL OPERATIONS

Wangensteen<sup>23</sup> vigorously champions aseptic anastomosis in gastrointestinal resections, and presents his experience with the closed method of anastomosis in 100 cases, comprising 83 gastric resections, 14 colonic resections and 3 miscellaneous cases. Only 1 case of postoperative gastric hemorrhage was encountered in the gastric resections, and the author attributes this to the use of the Hofmeister plan of anastomosis, whereby the more vascular part of the stomach is turned in, to ligation of visible subserosal vessels, to the use of a crushing clamp on the stomach and to the use of a coagulating current of the diathermy machine. The author admits that the closed anastomosis results in turning in a wider cuff of poorly approximated visceral wall, but points out that the commonly used Connell stitch is not free from this fault; he apparently does not consider this objection important. The report also includes an exhaustive discussion of details of preoperative and postoperative care. Wangenstein employs a bedside weighing scale in determining the state of hydration of poor-risk patients, a maneuver worthy of wide attention. He uses suction on a forked-type nasogastric catheter to prevent distention of the proximal jejunal loop after gastrojejunal anastomosis, the catheter being manipulated into the ascending and descending jejunal limbs at operation. He concludes that obstruction of the afferent loop in gastrojejunal anastomosis, without gangrene, is a neglected but significant cause of death after gastric resection.

Hoag and Saunders<sup>24</sup> consider the causes of obstruction following gastroenterostomy and sub-

total gastric resection, and propose jejunoplasty as a corrective operation. The procedure embodies the principle of the Finney pyloroplasty on the two limbs of the jejunum at the site of anastomosis, and the incision may be extended to the gastric wall in cases of contracted gastric stomach or marginal ulcer, according to the authors. Although most experienced surgeons have probably resorted to this procedure at one time or another, it is not to be considered the treatment of choice, as Allen notes in his discussion of the presentation. Possible jejunal necrosis and marginal ulceration, as well as the need for considerable operative manipulation in what may be a field of adhesions and inflammation and in what may be a depleted patient, are factors that weigh against routine adoption of jejunoplasty in this connection.

The rapidity of severe depletion in the presence of malfunctioning gastroenterostomy is stressed by Allen and Welch<sup>25</sup> in a comprehensive discussion of this problem. They advise early performance of jejunostomy in the treatment of the condition. The laparotomy wound is reopened for this purpose, and a simple purse-string type of jejunostomy is performed, the catheter being brought out through a stab wound. Provided the nutrition of the patient can be kept in satisfactory state, as by supplying a generous and complete dietary mixture through the jejunostomy tube, their figures show that spontaneous relief of the obstruction can usually be expected.

The use of a vitallium tube in the reconstruction of a strictured common duct is described by Pearse<sup>26</sup>. The tube is flanged, and the ends are flared slightly to fix it permanently in place. Since vitallium is notable for strength, lack of electrolysis and lack of local irritating effects, its superiority over the rubber catheter usually employed for common duct restoration may establish its place in this connection. As the author hastens to add, the value of such a vitallium tube is problematic if a gap is to be bridged between the ends of the duct.

McKittrick and Warren<sup>27</sup> describe a technical measure that has proved extremely helpful in their experience. As a preliminary to subtotal colectomy and other procedures requiring wide intraperitoneal exposure, the Miller-Abbott tube is passed. The small intestine is thus deflated and threaded on the tube beforehand, and at the operation not only is exposure of the operative field simplified, but the trauma involved in walling off loops of small intestine is obviated.

A point of concern to those interested in the surgery of the biliary tree is dealt with by Brunschwig and Clark.<sup>28</sup> In a case in which resec-

tion of the common duct for cancer was being performed, the main hepatic artery was found involved in the growth and had to be ligated and resected. Death of the patient ensued twenty-two days later, from what was thought to be liver failure. At autopsy, there was infarction of the right lobe of the liver, with no peritonitis and no pancreatitis. The authors report that Alessandri in 1937 was able to collect from the literature 10 cases of ligation of the hepatic artery in man, with fatal results in 6 and recovery in 4. He found also that in 18 reported cases in which one of the principal branches of the hepatic artery was ligated, lobar necrosis and early fatality resulted in 7. In man, recovery from ligation of the hepatic artery or its right or left branch apparently depends on the extent of collateral circulation present in the patient.

#### CARCINOMA OF THE AMPULLA OF VATER

This difficult surgical problem is now being attacked with a measure of success, made possible by advances in knowledge of the preoperative needs of the jaundiced patients.<sup>29</sup> Orr<sup>30</sup> reviews the 14 reported cases of resection of the duodenum and head of the pancreas for carcinoma of the ampulla, and adds a case of his own to the group. Five of the fifteen patients died after operation without leaving the hospital, and 3 died of metastases, 2 from stenosis of the cholecystgastrostomy stoma, and 1 from bile peritonitis. Four patients were still alive at the time of the report. Although disheartening, these results demonstrate the technical feasibility of excising the lesion, and will undoubtedly pave the way for more successful experiences. The best plan of surgical attack requires further study, bearing on such questions as the choice between one-stage and two stage procedures, and the optimal type of anastomosis between the obstructed biliary system and the gastrointestinal tract.

Moreland and Freeman<sup>31</sup> point out that two serious complications may follow resection of carcinoma of the ampulla of Vater—fatty degeneration of the liver and cholangitis. The evidence indicates that loss of the external pancreatic secretion can be successfully dealt with by such measures as a low fat diet and administration of lipocaine, pancreatic tissue or choline. These authors state that a high percentage of tumors in this region are of low grade malignancy. Occasionally, the growth involving the ampulla is sufficiently localized to permit transduodenal excision, although this method carries with it the danger of inadequate removal of tissue and is therefore not acceptable to surgeons experienced in the treat-

ment of cancer. River, McNealy and Ragins<sup>32</sup> report 3 cases of successful transduodenal excision of periampullary carcinoma, with reimplantation of the common and pancreatic ducts. Two of the patients developed stenosis of the common duct and required subsequent internal biliary drainage. The authors rightly stress the need for carefully determining the condition of the ampulla in operating on any patient with obstructive jaundice, so that no early ampullary growth will be overlooked.

#### POSTOPERATIVE PULMONARY COMPLICATIONS

Aspiration bronchopneumonia of varying severity is far commoner after surgical operations than is generally realized, according to Irons and Apfelbach.<sup>34</sup> In fatal cases, the true diagnosis is often missed because of failure to culture lung tissue, tracheal and stomach contents and blood. The characteristic alterations in the pulmonary parenchyma are most readily recognizable if the necropsy is performed within an hour or two of death. Their warning to the surgeon and anesthesiologist is timely, and points to the need—especially in upper abdominal operations—of preliminary evacuation of the stomach by intubation and maintenance of the head and thorax in a measure of dependency during the operation. In the prevention of postoperative pulmonary complications, Gordon<sup>34</sup> stresses the value of postoperative bronchial drainage by cough, posture or bronchoscopy. He regards bronchoscopy as a safe and simple procedure in well-trained hands, and advises early use of the measure in the treatment of postoperative pulmonary atelectasis.

Lindskog<sup>35</sup> presents clinical and experimental evidence bearing on the etiology of postoperative pulmonary complications. He states that bronchitis, atelectasis and pneumonitis continue to be a source of considerable morbidity and a cause of high mortality, especially in upper abdominal surgery. Lindskog finds that general anesthesia (Avertin) results in an immediate reduction in pulmonary subtidal volume by about 20 per cent before operation. A similar immediate reduction in subtidal volume was observed as a result of operation under local procaine anesthesia with preliminary morphine sedation. His studies led him to postulate a humoral theory for the etiology of postoperative pulmonary complications, according to which histaminelike substances are liberated from the sites of operation; these substances provoke secretion and bronchoconstriction in the lung. The stage is thus set for the action of mechanical factors that increase respiratory embarrassment.

#### POSTOPERATIVE CARE AND HOSPITALIZATION

Boyd<sup>36</sup> discusses the formation of renal calculi in bedridden patients, and reports 4 cases in which calcium phosphate stones formed rapidly and required surgical removal. One of the patients was being treated for delayed union of a fractured femur. Measures recommended in the prevention of such stones include acid-ash diet, avoidance of alkali, maintenance of large urine volume and frequent change of position in bed, with emphasis on assuming the prone position when possible.

A recent paper by Leithauser and Bergo<sup>37</sup> reminds me of a remark that the late Dr. E. Amory Codman once made to me on the subject of appendicitis. He predicted that the day would come when interval and prophylactic appendectomy would be performed through a McBurney incision under local procaine anesthesia in the surgeon's office, and the patient would be allowed to go home a few hours later. Leithauser and Bergo discuss their results in a group of 370 cases of appendectomy, in which early rising and ambulatory activity were practiced. The operation was for acute (nonperforative) and chronic appendicitis, and the average period of confinement to bed after operation was 1.5 days. The patients left the hospital by automobile and usually returned on the sixth day for the first dressing. In 66 laparotomies for other conditions, the average time of confinement to bed after operation was 1.9 days; in 18 cholecystectomies, the patients averaged 1.5 days in bed and 8.3 days in the hospital. In the entire group of 436 cases of laparotomy, no wound dehiscence, hernia, pneumonia, thrombophlebitis or other serious complications were observed (except hemorrhage in a gastrojejunal ulcer). The authors used the McBurney incision for appendectomy, and an oblique or transverse incision for cholecystectomy, the wound closure being made with chromic catgut and interrupted, buried steel-wire sutures for the fascia. Their "clinical results suggest the possibility that certain pathologic reflexes originating from the area of mechanical and chemical injury impair respiration and initiate a delay in peripheral circulation which leads to postoperative complications, and that strict confinement to bed favors the development of such complications."

Although few surgeons would care to adopt this program at present, even if it were acceptable to their patients, it must be admitted that the length of confinement to bed and hospital after operation is determined oftener by tradition than by criteria based on careful clinical research. Fur-

ther evidence on this important question should be obtained by studies in a number of clinics

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 27421

#### PRESENTATION OF CASE

*First Admission.* A twenty-month old Italian girl was admitted to the hospital for study.

The child was born at term, weighed 9 pounds, was breast fed for one year, with supplementary feedings after four months, and had been given unspecified amounts of orange juice. She had been well except for occasional coughs and colds until three months before admission, when pallor was noticed. Furthermore, the patient became restless and cried easily, and two weeks before admission, fever and indefinite pains in the hands and stomach were noticed. There had been no vomiting or diarrhea.

The family history was noncontributory. Neither of her two siblings was anemic.

On examination, the patient was well developed but flabby, with puffiness of the hands and feet, and pale, yellow skin. The scleras and mucous membranes were also very pale. The tonsils were large and cryptic; there was no lymphadenopathy. The lungs and the heart were normal except for a soft systolic murmur at the third left interspace. The abdomen was full; the liver was palpable 4 cm. below and the spleen 1.5 cm. below the costal margin. The extremities showed moderate enlargement of the epiphyses.

The urine on numerous occasions showed a + test for albumin and many white blood cells per high-power field. The red-cell count was 1,920,000 with a hemoglobin of 30 per cent, and the white-cell count 21,000 with 54 per cent polymorphonuclears, 36 per cent lymphocytes, 1 per cent monocytes, 7 per cent transitional cells, 21 per cent reticulocytes and 23 per cent nucleated red cells. Smears showed achromia, marked variation in size and shape, and many microcytes and macrocytes. The stools were guaiac negative.

The patient was given a high vegetable and fruit diet with 0.1 gm. of iron citrate each day. The hemoglobin rose to 50 per cent, and the red-cell count to 3,000,000, the smear remaining unchanged. The temperature on one occasion went to 105°F., and this was variously attributed to pyelitis and acute suppurative otitis media. The

patient was discharged three and a half weeks after admission.

*Final Admission* (eighteen years later). In the interval, the patient had been admitted to this and other hospitals on nine occasions, in addition to innumerable visits to the Out Patient Department.

A few months after discharge, the patient was seen again at this hospital, and a diagnosis of lymphatic leukemia made and x-ray treatment given. A year later, she was admitted to another hospital, where an enlarged liver and greatly enlarged spleen were noted, and a von Jaksch's syndrome diagnosed. In a few weeks, the patient was readmitted to that hospital with a temperature of 100°F.; an x-ray film of the chest suggested tuberculosis, and a von Pirquet test was positive. At another institution, the blood was reported to show a red-cell count of 4,180,000 with a hemoglobin of 60 per cent, and a white-cell count of 19,400, with 264,000 platelets and 19 per cent reticulocytes.

At the age of four, the patient had suffered from whooping cough, epistaxis and, later, bronchitis. The following year, a severe epistaxis ("a half cupful") occurred, followed by pain and swelling in both ankles lasting three days. At the last-mentioned hospital, a fragility test showed hemolysis beginning at 0.32 per cent and complete at 0.14 per cent, and an x-ray film of the chest showed the heart and supracardiac shadow to be increased in width. Treatment consisted of 1200 erythema skin units of x-ray.

At six years, the patient was said to have had lobar pneumonia and later during this year was seen at the same hospital complaining of cough and epistaxes of three weeks' duration. On examination she was well developed and nourished, but pale, with the spleen 6 cm. below the costal margin. The red-cell count was 3,700,000 with a hemoglobin of 53 per cent; the white-cell count was 26,500, and the smear as before. Two years later, she developed a prostrating cold and definite scleral icterus, with the liver 4 cm. below the costal margin; the blood picture, however, was slightly improved. At ten years, the icteric index was 20, and a Graham test was negative; some time later, the blood picture was noted to be essentially unchanged. During this period, the patient again contracted lobar pneumonia, and at the age of twelve was readmitted to this hospital complaining of a severe cold and pains in the abdomen and back, of four days' duration. The temperature was 103.6°F., and there were signs of consolidation at the left lung base. A fragility test showed hemolysis between 0.32 and 0.20 per cent. The spleen was not palpable, but following

recovery from the acute infection, both the spleen and the gall bladder, which contained stones, were removed. The spleen weighed 97 gm. and presented an unusual picture. Scattered throughout were numerous foci containing laminated deposits of brownish material, which stained for iron. These were largely enclosed by surrounding fibrous tissue and often showed foreign-body giant cells in contact with these deposits. Extending from these areas, strands of fibrous tissue stretched out and occasionally formed confluent areas of fibrous tissue. There was some increase of the perivascular fibrous tissue, but more marked increase of the perivascular elastic tissue. There was little if any intimal thickening. The lymphoid tissue was markedly reduced, and there was well marked congestion. Subsequently, a tonsillectomy was performed. The patient was discharged, the blood picture being unimproved.

It had previously been observed that occasional crises occurred during which the patient became more icteric, and the white cell count and hemoglobin fell to lower levels. She was readmitted to this hospital the same year in one of these crises and complained of headache and fever of five days duration. On examination, the temperature was 100°F, and the scleras icteric; dental caries were noted, and keloids had developed in the operative scars. The blood showed a red cell count of 1,900,000 with a hemoglobin of 45 per cent, and a white cell count of 14,600 with a normal differential. The red cells were as before, with 4 per cent reticulocytes and a large number of normoblasts. Gradually, the blood returned to its old level and did not change over the next two years, despite large doses of iron.

At fourteen, the patient suffered an acute febrile attack accompanied by pain and tenderness in all her joints. This lasted one month, and examination subsequently showed cardiac enlargement, with a continuous thrill in the neck and a continuous murmur in the right second interspace. Both the thrill and the murmur disappeared in dorsal decubitus. A rheumatic nodule was said to have been found in one foot.

For the next five years, the patient remained fairly well and even did light work. One year before her final entry, she was readmitted to this hospital with her stereotyped complaints of fever, cough without sputum and pain in the "stomach." The temperature was 104.6°F, and physical examination suggested right lower lobe pneumonia. An x-ray film showed evidence of consolidation at the right base, and the heart was still slightly enlarged. The red-cell count was 2,570,000, the hemoglobin 7.5 gm, the hematocrit 18 per cent,

the color index 0.9, the mean corpuscular volume 63 cu. microns and the mean corpuscular hemoglobin 26 microgm. Hemolysis began at 0.34 per cent and was complete at 0.14 per cent, control figures running 0.42 and 0.30 per cent, respectively. A sternal biopsy showed erythrogenic hyperplasia, with normoblasts predominating. The patient made a quick recovery on sulfapyridine, but three months later she was readmitted with exactly the same picture, even to the same lobe. The roentgenologist doubted the presence of pneumonia, but a blood culture yielded a Type 4 pneumococcus. The patient again recovered, and following discharge took a course of antipneumococcus vaccine and a course of liver extract injections. X-ray films of the hands and skull and also those of her sister showed no evidence of erythroblastic anemia.

The patient was finally admitted at the age of twenty, complaining of fever and pallor.

On examination, she was slightly obese and did not appear ill. The skin and scleras were slightly icteric. The heart and lungs were normal, except for fine rales and diminished breath sounds over the right base. The abdomen was normal.

The temperature was 105.8°F, the pulse 120, and the respirations 24.

The urine showed a specific gravity of 1.012, with a ++ test for albumin, and the sediment contained an occasional white blood cell and granular cast per high-power field. The blood showed a red cell count of 3,300,000 (260,000 of which were sickle cell forms) with a hemoglobin of 60 per cent, and a white cell count of 19,300 with 67 per cent polymorphonuclears, 23 per cent lymphocytes, 2 per cent normoblasts and 5 per cent myeloblasts. The serum van den Bergh and blood cholesterol, protein, nonprotein nitrogen and chloride were all normal, and two blood cultures were negative.

X-ray films of the chest showed no evidence of consolidation. There was a widening of the lower dorsal vertebrae that was suggestive of an old epiphysitis. Serial films, however, showed the development and progression of an unusual type of pneumonia involving first the left and then both lungs.

The patient was given sulfapyridine, then sulfathiazole, and while she was still on the drug, the temperature rose to 105°F, where it remained for some time. The apex impulse was heaving, and there were runs of bigeminy and trigeminy. An electrocardiogram showed a PR interval of 0.21 second. One observer noted cardiac enlargement and a systolic and a slight apical mid diastolic murmur, with accentuation of the pulmonic second sound. The right knee became swollen, the right

thumb painful. Finally, dyspnea became more and more severe, and the patient was placed in an oxygen tent. The temperature rose to 106°F., rales developed throughout both lungs, and a pleural friction rub was heard.

Death occurred one month after admission.

DIFFERENTIAL DIAGNOSIS

DR. THOMAS HALE HAM<sup>4</sup>: In summary this is a striking report of an Italian girl who was observed almost every year up to the age of twenty years, when she died apparently from pulmonary disease, which complicated a hemolytic anemia. The features of her clinical course were as follows. She had multiple episodes of hemolytic anemia associated with joint pains or pains in the

when removed at operation. The liver was moderately enlarged at all times.

The finding of sickle cells, together with the above evidence, confirms the diagnosis of sickle-cell anemia to explain the blood dyscrasia. Without the pathognomonic observation of sickle-shaped red cells, however, the following types of anemia would require differentiation: sickle-cell, erythroblastic (Cooley's), chronic hypochromic and familial microcytic. Certain distinguishing features<sup>1</sup> of these diseases are shown in Table 1. It is evident that hypochromic and familial microcytic anemia can be excluded because of the presence in this patient of jaundice, splenomegaly, increased reticulocytes and nucleated red blood cells. The distinction between Cooley's anemia and

TABLE 1. Distinguishing Features of Several Types of Microcytic Anemia.

FEATURE	SICKLE-CELL	ERYTHROBLASTIC (COOLEY'S)	CHRONIC HYPOCHROMIC	FAMILIAL MICROCYTIC
Inheritance of trait	Dominant	Recessive	None	Dominant
Predominant race or nationality	Negro predominately Mediterranean (Italian) occasionally.	Mediterranean	None	Mediterranean
Morphology of red blood cells	Sickled forms, increased reticulated and nucleated red cells, microcytosis and marked variation in size and shape.	Increased reticulated and nucleated red cells; microcytosis and extreme variation in size and shape	Less than 5 per cent reticulocytes; microcytosis and moderate to extreme variation in size and shape.	Less than 5 per cent reticulocytes; microcytosis and marked variation in size and shape.
Maximum resistance of red blood cells to hypotonic saline solution	Increased	Increased	Increased	Increased
Icteric index	Frequently elevated	Frequently elevated	Normal	Normal
Splenomegaly	Frequent	Usual	Rare	None
Bone changes	Occasional	Usual	None	Slight changes in skull

stomach and frequently with cough and fever. Coincident with several attacks of anemia, she had pulmonary complaints and signs interpreted usually as pneumonia. The laboratory observations revealed an anemia that developed rapidly on numerous occasions and reached a level of 1,900,000 red cells on one occasion. Sickle cells were demonstrated in the blood on her last hospital admission. An increased number of reticulated and nucleated red cells were always present during severe anemia. The red cells were microcytic, with marked variation in size and shape, and showed increased resistance to hemolysis in hypotonic solutions of sodium chloride. Icterus was observed clinically three times, and on one occasion the icteric index was 20. The leukocyte count was consistently elevated. The spleen increased in size from a few centimeters to 6 cm. below the costal margin. Subsequently, it disappeared clinically, and weighed only 97 gm.

sickle-cell anemia in this case is possible only by the observation of the sickle cells. Otherwise, it might be impossible to differentiate these two diseases, especially since the patient was of Italian parentage. One of the patient's parents must show sickle cells, since this trait is inherited as a Mendelian dominant. Neither parent was tested, however. The occurrence of sickle-cell anemia in white persons has been reviewed recently, with the report of 13 cases occurring in persons from Mediterranean countries, especially Italy.<sup>2</sup> This patient was Italian. The diagnosis of congenital hemolytic jaundice is ruled out in this case by the increased resistance of the red blood cells to hemolysis in solutions of hypotonic saline. There was no history of hemoglobinuria.

The characteristic symptoms of sickle-cell anemia are abdominal and joint pains in half the patients.<sup>3</sup> The predominant physical signs are jaundice and heart murmurs in over 70 per cent of the cases; in about 50 per cent, there is enlargement of the liver and heart; and in approxi-

<sup>4</sup>Associate in medicine, Harvard Medical School; associate director, Second and Fourth Medical Services (Harvard), and assistant physician, Thorndike Memorial Laboratory, Boston City Hospital.



mately one third of the cases there are pathologic changes in the lungs, ulcers or scars on the legs, fever and splenomegaly.<sup>3</sup>

Concerning the pathological physiology of sickle-cell anemia, Hahn and Gillespie,<sup>4</sup> in 1927, demonstrated that the sickled form of the red cells was produced by unsaturation of the hemoglobin by removal of oxygen from the cells. Recent observations,<sup>5,6</sup> have shown that red cells in the sickled form are strikingly more viscous than normally shaped cells. The viscosity increases as the partial pressure of oxygen is decreased, and the increased viscosity becomes manifest in vitro at about the oxygen tension of mixed venous blood. It is probable that such increases in viscosity occur in a patient with sickle-cell traits and produce a striking degree of stasis in the capillaries. This phenomenon may well account for the infarctions and abnormal destruction of red blood cells observed in certain of these patients.

These physiologic changes agree with observations that capillary blockage is the unit of pathology in sickle-cell anemia.<sup>7</sup> The pathological findings include the presence of sickle cells in dilated capillaries of the spleen, liver, kidney, lung and brain, together with thrombosis and infarction of these organs. The spleen of a child is usually enlarged, the capillaries and pulp being congested with sickled cells. Infarcts are common, and in older subjects the spleen decreases in size with fibrosis and may become extremely small. The lungs may be the site of multiple thromboses and infarcts involving many lobes. Thrombosis involving the brain may be extensive and may cause paralysis in a child as the first sign of sickle-cell anemia.

To return to the case under discussion, it is apparent that the patient had sickle-cell anemia, that the spleen, as described, showed evidence of diminished size, infarction, deposits of hemosiderin, fibrosis and congestion. The lung problem is of great importance, since it probably caused her death. At the age of three years, the child was considered to have tuberculosis, and at the ages of six, ten, twelve, eighteen and twenty the diagnosis of pneumonia was made. The best single explanation for the pulmonary lesion, especially that resulting in the atypical attack of pneumonia during the last illness, is multiple thromboses and infarcts of the lungs. The heart will probably show dilatation without valvular diseases.

DR. DONALD S. KING: We were interested in the lungs, and when I saw the patient I thought the diagnoses were Cooley's anemia and acute rheumatic fever. I believed at that time that the

joint changes were not associated with the anemia itself. We assumed that this was an atypical pneumonia, probably on a rheumatic basis. I am not at all sure that the pathologist would back that up, since this case was not quite typical of such a pneumonia. This explanation of Dr. Ham's sounds more reasonable.

#### CLINICAL DIAGNOSES

Acute rheumatic fever.  
Rheumatic pneumonia.  
Cooley's anemia.  
Sickle-cell anemia?  
Bronchopneumonia.

#### DR. HAM'S DIAGNOSES

Sickle-cell anemia.  
Fibrosis of spleen, with infarction, deposits of hemosiderin and congestion.  
Multiple thromboses and infarcts of lungs.  
Dilatation of heart.

#### ANATOMICAL DIAGNOSES

Sickle-cell anemia.  
Septicemia (hemolytic streptococcus).  
Rheumatic myocarditis, probable.  
Pericarditis, acute fibrinous.  
Acute and chronic pulmonary congestion.  
Pulmonary infarcts, multiple.  
Hyperplasia of the bone marrow.  
Operative scars: sternal biopsy; splenectomy; cholecystectomy.

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: There is a certain immoral aspect to the diagnosis of this disease, I think, because it is a common observation that if one looks at a fresh sample of blood one may not see sickling, but after delay it may become quite obvious, so that the intern who is slowest perhaps stands the best chance of making the diagnosis. This patient was in this hospital on numerous occasions, at the Children's Hospital several times and at the Huntington Memorial Hospital several times, and only twice in twenty years did anyone notice sickling. Once it was questioned at the Huntington Memorial Hospital, and at the last admission here it was definitely noticed by Dr. Louis Johnson. Several scores of people examined the blood and failed to note sickling. We had a chance to make the diagnosis when splenectomy was done but did not know enough to do it. We recognized at once that this spleen was unlike anything we had seen previously. The pulp looked like the spleen of hemolytic anemia, but there were degenerative changes

in the parenchyma, including foci of fibrosis that one would not expect to see in ordinary hemolytic anemia. The clinicians for the most part thought that the patient must have Cooley's anemia, and at nearly all admissions to this hospital that diagnosis was made. On what basis the diagnosis of lymphatic leukemia was advanced, I do not know. I think it is possible that she may at some time or other have had showers of nucleated red cells, and it is my experience that nucleated red cells are frequently counted as lymphocytes by the average medical intern. I do not know that that was so, but I should strongly suspect it. We eventually sent this spleen to the Johns Hopkins Hospital, where it was looked at by Dr. Arnold R. Rich, who at one glance recognized the lesion as one due to sickle-cell anemia and said it could be nothing else.

The other findings at autopsy are of some interest. The heart was a little dilated but probably not hypertrophic, weighing 300 gm., which is, I think, within normal limits for her age and size. There were no valvular lesions. On microscopic examination, a few small foci of round cells were found in the myocardium. I have backed and filled about these many times, but a few of them are certainly indistinguishable from Aschoff bodies. It seems to me that I must therefore make a diagnosis of active rheumatic fever. There was a fibrinous pericarditis, which may have been rheumatic in origin or may have been due to a terminal hemolytic streptococcus septicemia. The lungs presented a very unusual appearance. They were heavy and extremely red. When they were cut, almost no fluid exuded from them. There were also numerous obvious infarcts. The appearance was very much like that of the most extreme form of chronic passive congestion, the so-called "cyanotic induration of the lung" that one sees with severe mitral stenosis, yet this patient had a normal mitral valve. The infarcts were numerous, and were scattered all over the lung. Most of them tended to be fairly small, 1 to 2 cm. in diameter. The vessels within the infarcts showed thromboses. Elsewhere in the lung, it was very hard to find any thrombi.

An unusual feature about the autopsy was that the blood in all the vessels and in the major chambers of the heart itself was firmly clotted, making it very difficult to decide whether there might or might not have been ante-mortem clots, or whether coagulation had occurred immediately

after death, so that ante-mortem clots might easily have been obscured in this extensive post-mortem clotting process.

The picture in the lungs is a little reminiscent of rheumatic pneumonia but not very characteristic, and I think, in view of what Dr. Ham has pointed out to us, that it is much more reasonable to assume it to have been part of the sickle-cell anemia.

The bone marrow was hyperplastic, but to my eye showed no specific changes.

A PHYSICIAN: Would not x-ray treatment have modified the spleen somewhat?

DR. MALLORY: That was what we thought when we originally saw it—that the giant cells could be explained by the fact that radiation had been given. On the other hand, we do not in practice actually see these changes in patients whose spleens have been irradiated. We should have recognized the difference if we had known more about it. To anyone familiar with this disease who happened to think of the possibility, the diagnosis should have been obvious at any time but none of us even thought of it.

Have you any further comment, Dr. Ham?

DR. HAM: The wet-smear method of detecting sickle cells is usually satisfactory, but an immediate result may be obtained by the removal of oxygen from the red cells by equilibration of the blood with carbon dioxide or nitrogen. In this procedure, from 3 to 5 cc. of whole blood is introduced into a 250-cc. tonometer or Erlenmeyer flask equipped with a two-hole stopper. The blood is equilibrated with the gas for ten to fifteen minutes; a small amount of blood is then removed with a pipette, and a drop is placed immediately on a slide under a cover slip. This preparation is then examined for sickle cells. The blood cannot be dried in room air, since the cells are re-oxygenated and revert to the nonsickled form.

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# The New England Journal of Medicine

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## PHYSICIANS AND CIVILIAN DEFENSE

THE recent appearance of a handbook, *Organization Medical Division and Care of Injured Civilians*, issued by the Medical Division of the Massachusetts Committee on Public Safety, emphasizes preparation for civilian defense in America. Whether the plans so well laid will ever have to be called into being, no one can say, but all should be grateful that the Governor has seen fit to establish a mechanism for the protection of civilians. In America, so distant from the shores of Europe, it appears that danger is minimal, but many countries that have thus sought a way out of the effort of preparedness have been guilty of gross misjudgment and have suffered ugly and terrible consequences.

The Public Safety Committee of Massachusetts is composed of five divisions. Two of these, devoted to planning and publicity, are largely auxiliary and do not extend to any degree into the local communities. The Protection Division largely concerns itself with the work of the air-raid wardens and their many different tasks; 10,000 ARP Service men have already been through the schools, and 16,000 are now in training. The Public Services and Supplies Division has spread its network of regional directors and contact men throughout the State; their task deals with the maintenance of power, heat, light, communications, adequate food supplies and so forth. The Health and Social Services Division has three duties. The Public-Health Section looks after the health of people in preparation for war, the sanitary health measures during an emergency and the health measures that may be necessary after an emergency. The Social Services Section is concerned with activities promoting better morale, the social conditions in the environments of large army camps, the care of families rendered destitute by a grave emergency and the rehabilitation of individuals and populations after an emergency has passed. The Medical Division\* looks after the civilian from the time of injury until his restoration to active life.

The handbook was written to standardize and simplify the medical care of civilian casualties, whether from fire, bombs, bullets or shells, and with certain modifications, the British scheme has been followed. The authority for action when an "incident" occurs rests ultimately in the hands of the chief medical officer of the community. He sends to the scene a squad from the ARP Service. These men, already trained in first aid, enter the demolished houses and remove the injured. The walking wounded are guided, and those severely injured are carried on stretchers to a mobile medical first-aid post, which the chief medical officer has already established at the scene of disaster. Traction splints and bandages are applied, when necessary, and those persons who

\*Because of the experience in the recent war games, it has seemed wise to separate the Medical Section from the Public Health and Social Services sections, and the Medical Division is now a separate unit.

need hospitalization are immediately transferred by ambulance to the nearest hospital. The patients in hospitals in metropolitan areas are transferred the next day to large base hospitals in the rural districts, such as the Tewksbury State Hospital and various tuberculosis sanatoriums.

The chief medical officer and the local medical committee in each community have the responsibility of setting up these plans. In the large metropolitan areas, it has been suggested that the task be broken down so that one physician organizes the medical first-aid posts, another, ambulance transportation, and another, the hospitals. To assist the chief medical officers, regional directors have been appointed whose areas of jurisdiction largely correspond with those of the district medical societies.

The scheme for this vitally necessary undertaking is reasonable and workable, and is as good as if not better than that devised in any other state. All Massachusetts physicians should gladly and willingly complete the task that has been placed before them.

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## THE COMMONWEALTH FUND

THE Commonwealth Fund was established in 1918 by Mrs. Stephen V. Harkness to "do something for the welfare of mankind." According to its twenty-second annual report, grants amounting to more than \$2,000,000 were given for philanthropic purposes during the past year. A third of this total was devoted to medical research and medical education, and nearly half was contributed to various health services throughout the country, chiefly to rural health departments, and rural hospitals. Grants made in 1940 and in former years for medical research and education amounted to \$545,060, a large part being given to thirty-six medical-research projects at sixteen institutions. As an aid to medical education, the fund awarded fellowships for advanced study to seventeen teachers in medical schools. Special assistance was given to the teaching of preventive medicine at the Long Island College of Medicine, New York University College of Medicine, Tufts College Medical School, Tulane University of Louisiana School

of Medicine and Vanderbilt University School of Medicine, and to the Department of Psychiatry at the University of Louisville. Other significant contributions went to local public-health services and rural hospitals.

Of particular interest in the current report, however, is the grant of \$135,000 to meet special war needs abroad. Gifts were made to the American Red Cross and the British War Relief Society. The Child Guidance Council supported by the fund has proved its usefulness by its work among the children evacuated from London and other cities.

The Commonwealth Fund has indeed adhered to its motto: "To do something for the welfare of mankind." Its indispensable support of numerous efforts to solve the problems of human welfare and happiness and its contribution to the relief of suffering in war-torn Europe echo the motive of the fund's foundation in 1918. Its achievements remain not only a tribute to the selflessness of its founder and the zeal of its directors but also an inspiration to private philanthropy.

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## OBITUARY

### GERALD BLAKE

1880-1941

The tradition of medicine was strong and deep in "Jerry" Blake. His father and his brother were doctors. His father was the much beloved Dr. John G. Blake, for many years on the staff of the Boston City Hospital, a fine general practitioner of the old school, who, when he moved to Boston's Back Bay, liked to recall the older days of Boston's South End. His mother was well known to the readers of the *Boston Transcript* under the initials of "M. E. B."

He grew up in a large family, mostly boys. All were gay, with a family talent for singing songs of infectious mirth and of interminable verses. One readily recalls the "Whizz Fish" and the "Bummers Hotel."

In Harvard College, at a time when the Harvard Band was more a manifestation of nearly spontaneous undergraduate enthusiasm than today's expression of nearly musical talent, "Jerry" occasionally beat the bass drum because the band had to have a bass drummer.

In the Harvard Medical School, "Jerry" was the best liked man in the Class of 1905—friendly,

hard working, intelligent, modest but effectively loyal led him to choose an internship at the Boston City Hospital. He then entered service in Boston. Of course, with his ability, integrity and his personality, he was eminently successful professionally. He greatly admired medical research, but his busy, full life of practice left him no time, and indeed his modesty and honesty made him feel that he was not fitted for research. In any event, his patients and his family came first.

He went through the various stages on the teaching staff of the Massachusetts General Hospital, and for a number of years held the position of visiting physician. The ward patients loved him for his sympathy, his humor and his excellent bedside manner. The interns and residents learned much from him that they had not found in books or lectures. On ward rounds one morning, an over-tired intern delivered a long dissertation on some topic not particularly related to the patient beside whose bed they had stopped. The patient became very apprehensive over the earnestness of the young man and over the medical jargon. He patted the patient and looked kindly at the intern. Finally, he quietly said to the intern, who had paused to get his breath: "What kind of razor do you use? You get a useful close shave."

Over a dozen years ago, Jerry had a severe illness. After this, he had albuminuria and a microscopic hematuria, both of which persisted. His blood pressure slowly began to climb. He had attacks of pulmonary apoplexy, several episodes of minor cerebral accidents and a coronary embolism. After the attack of coronary thrombosis he developed angina, which plagued him daily in his last years of his life. He never complained; he insisted on continuing his large active practice, which he did with undiminished excellence. He grew thin because eating gave him angina. He still had the picture of him, tall and thin, slowly wasting—by this time he had acquired a Parkinsonian syndrome—up the Phillips House steps. "How are you, Jerry?" His face would light up with his old delightful smile, and the answer would be, "Oh, fine." And this kept up for months and months, until his complete incapacity made him consent to take his vacation ten days ahead of the time he had stipulated for himself, despite pleas and protests. On his way to his holiday, he developed his final coronary thrombosis. A great practitioner and a lovable personality had become a hero for years. "Jerry" had had what it takes to make a hero.

R I L

## MEDICAL EPONYM

### KOPLIK'S SPOTS

This sign was described by Henry Koplik (1858-1927) in the *Archives of Pediatrics* (13: 918-922, 1896), in an article entitled, *The Diagnosis of the Invasion of Measles from a Study of the Exanthema as It Appears on the Buccal Mucous Membrane*.

One of the most, if not the most, reliable sign of the invasion of measles has fully failed to receive due attention. If we look in the mouth at this period [during the first twenty-four to forty-eight hours of the invasion], we see a redness of the fauces, perhaps a few spots on the soft palate. On the buccal mucous membrane and the inside of the lips, we invariably see a distinct eruption. It consists of small irregular spots, of a bright red color. In the center of each spot, there is noted, in strong daylight a minute bluish white speck. These red spots, with accompanying specks of a bluish white color, are absolutely pathognomonic of beginning measles, and when seen can be relied upon as the forerunner of the skin eruption. As the skin eruption begins to appear and spreads, the eruption on the mucous membrane becomes diffuse. The buccal eruption begins to fade even while the skin exanthema is at its height. In cases where this eruption has been absent, I have always found that my exclusion of a probable attack of measles was correct.

R W B

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

#### PREMATURE SEPARATION OF THE PLACENTA, FOLLOWED BY FATAL SHOCK AND HEMORRHAGE

A thirty year-old para VIII who had been followed adequately during pregnancy began to flow very freely at term, and was consequently sent into the hospital.

The previous seven pregnancies had terminated in normal deliveries.

On entry the patient had a tender uterus and was flowing freely. No mention was made whether the fetal heart was audible. Vaginal examination at this time showed that the cervix was dilated sufficiently to admit two fingers, and no placenta was felt, no treatment was given. Two hours later, a cesarean section was performed, after a diagnosis of premature separation of the placenta had been made. The placenta was found lying free in the uterine cavity, and a stillborn fetus

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, Secretary, 330 Dartmouth Street, Boston.

was delivered. The patient's condition was apparently very poor at the end of the operation. She was given intravenous glucose but was not transfused. Four hours after the operation, she died, apparently from shock and hemorrhage.

*Comment.* This case illustrates quite well how cases of premature separation of the placenta should not be treated. It is a little unusual in prematurely separated placentas to have excessive external hemorrhage; more frequently, external hemorrhage is slight, and internal hemorrhage is great. It would have been very much better to have treated this patient conservatively. She was a multipara, and although not in labor, she certainly had a cervix that was approximately at term, since it is reported that the cervix was dilated to admit two fingers. The conservative treatment would have consisted in tight cervical and vaginal packing, a Spanish windlass, transfusion and small doses of pituitary extract. Frequently, cases of separated placenta are associated with increased blood pressure and albuminuria, but these were not present in this patient. In primiparas when the fetus is still alive cesarean section may be the operation of choice. In these cases, only 1-minim doses of pituitary extract should be used at intervals of approximately an hour until labor is established. The mortality from this complication when so treated has dropped very appreciably, but conservative treatment cannot guarantee against fatality. If the patient is exsanguinated before the treatment is instituted or if she is extremely toxic, with complete suppression of the urine, nothing can prevent a fatal outcome. The shock of an abdominal operation on a patient such as this is often too much for Nature to combat.

## MISCELLANY

### BOSTON UNIVERSITY SCHOOL OF MEDICINE OFFERS HOSPITALIZATION SERVICE

Hospitalization service will be offered to students of Boston University School of Medicine throughout the present academic year for a five-dollar fee or a donation to the blood bank, President Daniel L. Marsh and Dean Bennett F. Avery of the school recently announced. Under the hospitalization plan, the medical students will receive complete medical care during the school year. The program has been developed under a new agreement, now going into effect with the Massachusetts Memorial Hospitals, to aid medical students needing hospital care throughout the academic year.

## NOTE

Dr. C. Sidney Burwell, dean of the Harvard Medical School, recently announced that Dr. Derek E. Denny-Brown, of London, had arrived in Boston from England

to take up his duties as professor of neurology and director of the Neurological Unit, Boston City Hospital. Dr. Denny-Brown's appointment dates from September, 1939, but during the interval he has been on leave of absence serving as a major in the British Medical Corps. Since January, 1940, he has been the officer in charge of the Medical Division, Military Hospital for Head Injuries, in England. In his combined duties here he will take active part both in the teaching of medical students and in the care of the sick in the City of Boston.

## CORRESPONDENCE

### PREMARITAL HEALTH EXAMINATIONS

*To the Editor:* The Department of Public Health has sent to all Massachusetts physicians a letter describing their responsibilities under the new premarital health-examination law. It is requested that the *Journal* print a list of the laboratories at present approved by the department for performing serologic tests for syphilis, and certain sections of the general marriage laws with which physicians should be familiar.

The blood specimen for serologic examination for syphilis should be sent to the Wassermann Laboratory, 25 Shattuck Street, Boston, or to a laboratory approved by the department. The following laboratories have so far been approved:

- Boston
  - Beth Israel Hospital
  - Boston Health Department
  - Leary Laboratory
  - Massachusetts General Hospital
  - Peter Bent Brigham Hospital
- Brockton
  - Health Department
- Fall River
  - Truesdale Hospital
- Fitchburg
  - Burbank Hospital
- Holyoke
  - Providence Hospital
- Montague
  - Farren Memorial Hospital
- New Bedford
  - St. Luke's Hospital
- Pittsfield
  - St. Luke's Hospital
- Springfield
  - Mercy Hospital
- Tewksbury
  - State Infirmary
- Worcester
  - City Hospital
  - St. Vincent Hospital

Presumably the city laboratories will do blood tests only for local physicians, and the hospital laboratories only those of patients in the hospitals or outpatient departments.

The following sections taken from the Marriage Laws answer most of the questions which marriage applicants will ask physicians:

## General Laws, Chapter 207 (as amended)

Section 11 No marriage shall be contracted in this commonwealth by a party residing and intending to continue to reside in another jurisdiction if such marriage would be void if contracted in such other jurisdiction, and every marriage contracted in this commonwealth in violation hereof shall be null and void

Section 12 Before issuing a license to marry a person who resides and intends to continue to reside in another state, the officer having authority to issue the license shall satisfy himself, by requiring affidavits or otherwise, that such person is not prohibited from intermarrying by the laws of the jurisdiction where he or she resides

Section 19 Persons intending to be joined in marriage in the commonwealth shall, not less than five days before their marriage, cause notice of their intention to be filed in the office of the clerk or registrar of the town where each of them dwells, or, if they do not dwell within the commonwealth, in the office of the clerk or registrar of the town where they propose to have the marriage solemnized. In computing the five-day period specified in this section and in determining the fifth day referred to in section twenty eight, Sundays and holidays shall be counted

Section 20 (as amended by Chapter 127, Acts of 1933) The clerk or registrar shall require written notice of intention of marriage, on blanks furnished by the state secretary, containing such information as is required by law and also a statement of absence of any legal impediment to the marriage, to be given such clerk or registrar under oath, by both of the parties to such intended marriage if both dwell in his town, or, if the parties dwell in the different towns within the state, or if one dwells outside the state, by the party dwelling in his town, or, if both dwell outside the state, by both such parties, provided that if a registered physician makes affidavit to the satisfaction of the clerk or registrar that a party so required is unable, by reason of illness, to appear, such notice may be given on behalf of such party, by his or her parent or legal guardian, or, in case there is no parent or legal guardian competent to act, by the physician certifying to the illness, or by the other party irrespective of such other party's residence. The oath to such notice shall be to the truth of all the statements contained therein whereof the party subscribing the same could have knowledge, and may be given before the clerk or registrar or before a regularly employed clerk in his office designated by him in writing and made a matter of record in the office. No fee shall be charged for administering such oath. In towns having an assistant clerk or registrar, he may administer the oath.

PAUL J. JANNAUH, M.D.  
Commissioner of Public Health

State House  
Boston

## NOTICES

## BOSTON LYING IN HOSPITAL

There will be a meeting of the Journal Club of the Boston Lying in Hospital on Thursday, October 30 at

8 p.m. Dr. Norris W. Vaux, professor of obstetrics at Jefferson Medical College of Philadelphia, will speak on 'Some Local Uses of Estrogenic Hormones in Obstetrics and Gynecology'

NEISSERIAN MEDICAL SOCIETY  
OF MASSACHUSETTS

The annual meeting of the Neisserian Medical Society of Massachusetts will be held on Wednesday, October 29, at 7 p.m., at the Hotel Kenmore, Boston

## PROGRAM

Dinner

Election of officers

Speaker Ernest B. Howard, M.D., director, Division of Genitoinfectious Diseases, Massachusetts Department of Public Health

Round Table Discussion Gonorrhea and National Defense "

## CARNEY HOSPITAL

The monthly clinical meeting and luncheon of the staff of the Carney Hospital will be held in the auditorium of the Carney Hospital on Monday, October 20, at 11 30 a.m.

## PROGRAM

Case Reports

Clinicopathological Conference.

Discussion by Drs. William Flynn, Joseph O'Brien, Norman A. Welch and Roger C. Graves

Physicians and medical students are invited to attend

## JEWISH MEMORIAL HOSPITAL

A diagnostic therapeutic conference will be held at the Jewish Memorial Hospital on Thursday, October 23, at 11 a.m. Dr. Elliott P. Joslin will speak on 'Diabetic Problems'

Interested physicians and medical students are cordially invited to attend

## EDWARD K. DUNHAM LECTURES

The Faculty of Medicine of Harvard University has announced that the following lectures, prepared by Dr. Rudolf Schoenheimer, formerly associate professor of biological chemistry, Columbia University College of Physicians and Surgeons, will be delivered by Professor Hans T. Clarke, under the Edward K. Dunham Lecture ship for the Promotion of the Medical Sciences

Tuesday, October 28 The Chemical Reactions of the Body Fats

Wednesday, October 29 The Chemical Reactions of the Body Proteins

Thursday, October 30 The Dynamic State of the Body Constituents

These lectures are scheduled for 5 p.m. at the Harvard Medical School Amphitheater, Building C

## NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The regular monthly meeting of the New England Society of Physical Medicine will be held on Wednesday evening, October 22, at the Hotel Kenmore, Boston.

The council will meet at 6:00, and an informal dinner will be held in the Empire Room at 6:30. At 8:00, Dr. Augustus Thorndike, Jr., will speak on "The Effects of Physical Therapy on Athletic Injuries."

All members of the medical profession are cordially invited to attend.

## CUTTER LECTURE

Sir William Wilson Jameson, chief medical officer, Ministry of Health, London, will give the Cutter Lecture on Preventive Medicine at the Harvard Medical School on Wednesday, October 22. His subject will be "Public Health in Britain at War," and the lecture will begin at five o'clock in the amphitheater of Building E. These lectures have been given annually since 1912. The medical profession, medical and public-health students and others interested are invited to attend.

## BOSTON DOCTORS' SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse, under Alexander Thiede, every Thursday at 8:30 p.m. at Station WMEX, 70 Brookline Avenue, Boston. Those interested in becoming members should commu-

nicate with Dr. Julius Loman, 520 Beacon Street, Boston (KEN 3200 or LON 2155).

## THOMAS WILLIAM SALMON MEMORIAL LECTURES

The Salmon Committee on Psychiatry and Mental Hygiene invites the members of the medical profession and their friends to the ninth series of Thomas William Salmon Memorial Lectures.

This series will be given by Dr. Robert D. Gillespie, psychiatric specialist of the British Royal Air Force. The lectures will be given on November 17 and 18 in New York City, November 19 in Toronto, November 21 in Chicago, November 22 in New Orleans, November 27 in San Francisco and November 30 in Philadelphia. Dr. Gillespie will speak on "Psychoneuroses in Peace and War, and the Future of Human Relationships."

## MASSACHUSETTS PUBLIC HEALTH ASSOCIATION

A meeting of the Massachusetts Public Health Association will be held at the Commander Hotel, Cambridge, on Thursday, October 30.

The section meetings will be held at 3 p.m. A buffet supper (\$1.25 per cover) will be served at 6 p.m. Following the general business meeting at 7 p.m., seven experts will conduct a symposium, "New Developments in Prophylactic Immunizations."

## RECEPTION FOR DR. HYMAN MORRISON

A reception and tea in honor of Dr. Hyman Morrison will be given October 19, at 2:30 p.m., at the Beth Israel

Hospital, celebrating his sixtieth birthday. A sum of money has been collected for the purpose of establishing the Hyman Morrison Laboratory for Research in Medicine at the National University, Jerusalem. A check for this purpose will be presented to Dr. Morrison on this occasion.

## SOCIETY MEETINGS AND CONFERENCES

### CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, OCTOBER 19

#### MONDAY, OCTOBER 20

- \*11:30 a.m. Monthly clinical meeting and luncheon of the staff, Carney Hospital auditorium.
- 12:15-1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

#### TUESDAY, OCTOBER 21

- \*9:00-10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.
- \*12:00 m. The Physician in National Defense. Dr. Donald E. Currier. South End Medical Club, headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston.
- 12:15-1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital amphitheater.

#### WEDNESDAY, OCTOBER 22

- \*9:00-10:00 a.m. Acne, Hirsutism and Menstrual Disorders. Dr. C. H. Lawrence. Joseph H. Pratt Diagnostic Hospital.
- 10:00 a.m. John T. Bottomley Society. Carney Hospital.
- \*12:00 m. Clinicopathological conference. Children's Hospital.
- \*5:00 p.m. Public Health in Britain at War. Sir William Wilson Jameson. The Cutter Lecture. Harvard Medical School, amphitheater of Building E.
- \*8:00 p.m. The Effects of Physical Therapy on Athletic Injuries. Dr. Augustus Thorndike, Jr. New England Society of Physical Medicine, Hotel Kenmore, Boston.

#### THURSDAY, OCTOBER 23

- \*8:30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Peter Bent Brigham Hospital.
- \*9:00-10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.
- \*11:00 a.m. Diabetic Problems. Dr. Elliott P. Joslin. Jewish Memorial Hospital.

#### FRIDAY, OCTOBER 24

- \*9:00-10:00 a.m. Physical Fitness in Late Maturity. Dr. Robert T. Monroe. Joseph H. Pratt Diagnostic Hospital.

#### SATURDAY, OCTOBER 25

- \*9:00-10:00 a.m. Presentation, with discussion, dispensary and district cases. Joseph H. Pratt Diagnostic Hospital.
- \*Open to the medical profession.

OCTOBER 13-24. 1941 Graduate Fortnight of the New York Academy of Medicine. Page 834, issue of May 8.

OCTOBER 17. New England Society of Psychiatry. Page 600, issue of October 9.

OCTOBER 19-23. American Academy of Ophthalmology and Otolaryngology. Page 350, issue of August 28.

OCTOBER 28-30. Edward K. Dunham Lectures. Page 635.

OCTOBER 29. Neisserian Medical Society of Massachusetts. Page 635.

OCTOBER 29-30. New England Postgraduate Assembly. Pages vi and vii.

OCTOBER 29-NOVEMBER 1. Association of Military Surgeons. Page 473, issue of September 18.

OCTOBER 30. Journal Club meeting, Boston Lying-in Hospital. Page 635.

OCTOBER 30. Massachusetts Public Health Association. Notice above.

NOVEMBER 3-7. American College of Surgeons. Page vii, issue of July 31.

NOVEMBER 5-6. American Conference on Industrial Health. Page 473, issue of September 18.

NOVEMBER 13. Pentucket Association of Physicians.

NOVEMBER 17-19, 21-22, 27 and 30. Thomas William Salmon Memorial Lectures. Notice above.

JANUARY 3. American Board of Obstetrics and Gynecology. Page 473, issue of September 18.

JANUARY 10-11. Forum on Allergy. Page 392, issue of September 4.

APRIL 6-10. American Congress on Obstetrics and Gynecology. Page 600, issue of October 9.

APRIL 20-24. American College of Physicians. Page 996, issue of June 5.

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# The New England Journal of Medicine

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## THE ROLE OF THE ROENTGENOLOGIC EXAMINATION IN THE DIAGNOSIS OF INTESTINAL OBSTRUCTION\*

EUGENE P. PENDERGRASS, M.D.†

PHILADELPHIA

IN studying patients who have symptoms suggestive of intestinal obstruction, some of the problems that the clinician must answer if possible include the following: Is an obstruction present? Does it involve the stomach, the duodenum, the small intestine, the colon or a combination of these organs? Is the obstruction single or multiple? Is the obstruction complete or incomplete? What is the cause of the obstruction? Is it an acute occlusion, or is it the final closure of a slowly developing lesion?

The most valuable aid on which the clinician may rely is probably the correct interpretation of observations gleaned from a carefully planned roentgenologic examination of the abdomen or the gastrointestinal tract. The discussion of such observations is limited, for the most part, to those concerning the small intestine and colon.

### PRESENCE OF OBSTRUCTION

Patients with obstructive lesions in the intestinal tract, some of which are almost complete, do not always present classic symptoms. Occasionally, this is true of a lesion involving the pylorus and duodenum. In such cases, the diagnosis can be made only after the patient has had a roentgenologic study of the gastrointestinal tract.

As a rule, the patient with symptoms of an acute abdominal condition is referred to the radiologist for a survey examination of the abdomen. If the condition is such that he can be moved with safety, examination of the abdomen includes a fluoroscopic study in the horizontal and semierect positions. The advantage of such a procedure is to determine the extent of the movement of the domes of the

diaphragm and to make, if necessary, roentgenograms of important fluoroscopic observations.

The minimum requisite of such a study is a roentgenogram of the abdomen in the anteroposterior position. Additional roentgenograms that may reveal valuable information are as follows: posteroanterior and lateral films with the patient in the recumbent position; anteroposterior or posteroanterior films with the patient lying on the left or right side; and anteroposterior or posteroanterior films with the patient in the erect position. Whenever possible, the shadows of the domes of the diaphragm should be seen on the roentgenogram, and a lateral view of the pelvic region should be available for study of gas shadows in the rectum.

The purpose of the survey is to determine the presence and location of any demonstrable gas in the intestinal tract or abdomen, the presence or absence of muscle shadows and the preperitoneal fat lines, and to locate if possible any abnormal soft-tissue lesions.

Gas is present throughout the alimentary canal, but under normal conditions (except in infants and very small children) one does not see gas shadows in the roentgenograms of the small intestine. In the stomach and colon, gas shadows are found frequently in roentgenograms of the abdomen. Wangenstein<sup>1</sup> explains the inability to see the gas shadows in the small intestine as being due to the intimacy of the admixture between the fluid and gas. Under conditions of stasis, however, the gas separates from the fluid and can be demonstrated readily.

According to Wangenstein, gas in the obstructed intestine consists of the gas produced by digestive processes, that diffusing from the blood into the intestinal lumen, and swallowed atmospheric air. Under experimental conditions, swallowed air accounts for 68 per cent of the gas shadows found

\*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1941.

†From the Department of Radiology, Hospital of the University of Pennsylvania.

1Director, Department of Radiology, Hospital of the University of Pennsylvania.

in intestinal obstruction, the remainder of the shadows being due to the other two sources. Wangensteen says that one can demonstrate abnormal gas shadows on the roentgenograms of experimental obstructive lesions after four or five hours. It is not known how long it takes for gas shadows to become apparent in intestinal obstruction in human beings, but it is common knowledge that chemical irritants such as Diodrast cause visible gas shadows in the small intestine in a few minutes.

Abnormal gas shadows in the small intestine and colon may occur as a result of a variety of conditions, most of which the radiologist must bear in mind to make a careful correlation of the roentgenologic and clinical observations before he attempts to arrive at a provisional diagnosis. Some of the things, other than intestinal obstruction, that produce abnormal gas shadows and modify the roentgenologic signs are as follows: morphine and many other sedative drugs; peritoneal irritation from any cause, such as retroperitoneal hemorrhage due to an injury; dysentery and many bacterial and chemical irritants, and nutritional deficiencies; a ruptured graafian follicle; and general conditions, such as diabetes and sickle-cell anemia.

If the radiologist and the clinician, after study of the data, conclude that the abnormal gas shadows are due to an obstruction, the next problem to decide is where it is.

#### LOCATION OF OBSTRUCTION

With the exception of obstruction due to hypoproteinemia, it is not the purpose of this presentation to discuss obstructive lesions involving the stomach and duodenum.

The radiologist is frequently called on to examine patients who have had reconstructive operations performed on the stomach. Some of these patients continue to vomit, and after a barium meal, the stomach may not empty for many hours, and the radiologist and surgeon often conclude that the patient has a mechanical obstruction due to adhesions or some defect resulting from the operation.

My experience and that of Barden et al.<sup>2</sup> indicate that the stomach frequently empties very slowly for approximately three weeks after operation, owing to the influence of operative trauma, hypoproteinemia and possible vitamin deficiencies. After the return of such factors to normal, the stomach empties without the slightest difficulty. If such factors account for the patient's symptoms and are recognized, an unnecessary operation may be prevented.

In the study of roentgenograms of the abdomen,

experience has shown that if the gas shadows are limited to the colon, and the symptoms are acute, the obstruction is likely to be found in that organ. Wangensteen,<sup>1</sup> Rigler and Lipschultz<sup>3</sup> and many others have called attention to this observation in the past. Wangensteen states that the ileocecal sphincter and valve operate in the manner of a check valve, allowing gas and fluid from the small intestine to be swept into the colon, but that regurgitation is prevented by the sphincter. In my experience, the small bowel rarely participates in a colonic obstruction unless the process is chronic or extends beyond the confines of the colon, or unless the lesion is associated with a spreading infection.

A survey examination of the abdomen may afford all the information necessary to diagnose and locate the position of a colonic obstruction. If it does not, a barium enema may be indicated to meet the requirements of the surgeon who wishes to know the nature of the pathologic process and the degree and position of the obstruction. Occasionally, it is impossible to administer a barium enema because of the patient's inability to retain it. At other times, the illness of the patient and the severe distention of the colon make one hesitate to subject the patient to the manipulation that such an examination necessitates, owing to the danger of perforation of an already overdistended and necrotic bowel.

If the abnormal gas shadows are limited to the colon, the obstruction is likely to be mechanical. I have seen only one patient who suffered from a paralytic distention of the colon produced by a spinal-cord lesion that simulated and had to be differentiated from an organic obstruction. As a rule, a paralytic ileus causes distention of the small and large intestine and offers no difficulty in the differential diagnosis.

Rigler and Lipschultz<sup>3</sup> describe the roentgenologic signs that they consider helpful in making a diagnosis of volvulus of the sigmoid. These signs include the increased size of the sigmoid, most of the lumen of which is found high up in the abdomen outside the pelvis and to the right of the midline, the presence of unusual amounts of fluid and the demonstration of a double point of obstruction. A barium enema may be necessary to assist in determining the diagnosis. In a patient with volvulus whom I studied, the administration of the enema was greatly facilitated by having the patient get in the knee-chest posture. A similar position is recommended in all patients who have large pelvic masses.

If the patient has a primary lesion of the colon, such as diverticulitis or an infected carcinoma, the

small intestine, in addition to the colon, is frequently distended. The use of the stethoscope assists in diagnosing or excluding a paralytic ileus, and a barium enema frequently helps to determine the nature of the pathologic process. This is especially significant when the gas shadows of the small intestine simulate the haustral markings in the colon.

A colonic lesion is apter to result in perforation than a lesion of the small intestine is, and the cecum is more vulnerable to distention than other portions of the colon. Roentgenograms are made in the erect and the lateral decubitus positions to demonstrate free gas in the peritoneal cavity. Thick shadows of the intestinal walls may be due to peritonitis. The loss of the shadow of the preperitoneal fat line or the absence of the lumbar-muscle shadows should be evaluated, because such observations may indicate peritonitis.

The clinical signs of obstruction of the small intestine are much more definite than those of colonic obstruction. The observation of varying amounts of distention of the small intestine is the only roentgenologic evidence of such a condition. Until a few years ago, the radiologist without the aid of the opaque meal was unable to demonstrate the site and nature of the obstructive lesion. Now, through the agency of a multiple-lumened tube,<sup>4</sup> it is possible not only to intubate the small intestine but also to determine the position and nature of the obstructive lesion and the completeness of the obstruction.

The procedure of intestinal intubation in obstruction consists in the passage of the tube down the intestine until it stops, or, if the obstruction is paralytic, until the obstruction has been overcome. In mechanical obstruction, it is possible to inject a thin suspension of barium and determine whether one is dealing with an intrinsic lesion, such as a tumor, or an extrinsic lesion, such as adhesions. If, after the barium has been injected, the opaque suspension regurgitates proximally along the barrel of the tube, one suspects an obstructive lesion. Colonic lesions are likely to cause the tube to stop progressing in the small intestine in the right iliac fossa owing to spasm of the ileum. Experience leads me to suggest that whenever the tube stops in the ileum one should administer a barium enema to diagnose or exclude a colonic lesion before making a diagnosis of an organic ileal obstruction.

One of the most frequent errors in interpretation has to do with the false impression of progression of the barium that is injected into the intestine by way of the Miller-Abbott tube. The sequence of observations may be as follows: the double-lumened tube stops in the right lower quadrant;

the tip of the tube, in progressing to that point, has allowed the small intestine to telescope over the barrel of the tube; the balloon is deflated and 20 cc. of thin barium suspension is injected into the intestine; following the deflation of the balloon, the portion of the small intestine that has telescoped over the tube begins to readjust itself, thus allowing barium to escape beyond the tip of the tube even in the presence of a complete obstruction. Obviously, the barium does not progress beyond the point of complete obstruction, but the apparent progression of barium is due to the unraveling of the bowel from the tube. Evidence of pleating of the tube proximal to the balloon should always be looked for, and the patient should continue to swallow the tube until pleating has disappeared before one may be sure that the tip will not retreat up the intestine on deflation of the balloon.

The procedure of intubation has many other important functions to fulfill. Some of the purposes that have been recorded by Abbott<sup>5</sup> include the following: to determine the nature of the obstruction; to determine fluid and salt loss; to relieve colic and vomiting by decompression of the distended bowel; to return peristalsis by relief of overdistention; to render operations elective rather than emergency procedures; to facilitate surgical procedures (especially in multiple obstruction); and to decrease the likelihood of postoperative leaks.

Many objections have been raised to the procedure of intubation. The first is the time required to pass the tube. A physician experienced in intubation is essential. In recent months, Abbott<sup>6</sup> has been able to pass the tube into the duodenum much more rapidly by the assistance of the rigidity produced by a piano wire placed in the double-lumened tube. Secondly, it is not always possible to aspirate the contents from the intestine. Thirdly, the tube is sometimes found to be obstructed after it has been passed. The employment of a nurse to keep the tubes clean should obviate any such complaint. Fourthly, in colonic lesions, spasm of ileum may cause faulty obstruction of the tube. Fifthly, the procedure may fail to decompress the colon, or the small bowel in cases with multiple obstructions. Finally, there is the delay in operation due to the loss of time while intubation is being attempted.

There are many suggestions that have been and might be made to help one overcome the objections just detailed, but most of these drawbacks are easily obviated if an experienced team is developed in each hospital. When that time comes, the high mortality of intestinal obstruction will become a relic of the past.

## EXTENT OF OBSTRUCTION

Most of the incomplete obstructions are studied by either the barium meal or enema, or both; they are often unsuspected. Intestinal obstruction after operation is often incomplete, and frequently occurs as a result of inflammatory adhesions or of adhesions in addition to inflammation or chemical imbalance in the tissues. If such a patient has a partial obstruction of the small intestine the Miller-Abbott tube, if passed, will stop at the site of the obstruction. Then, if barium is injected through the tube, it will progress in a caudal direction, and the nature of the obstructing condition can often be diagnosed. Such information is extremely valuable.

If the small bowel is completely obstructed, nothing will pass through it, and if barium is injected through a Miller-Abbott tube, it will regurgitate along the barrel of the tube. The complete obstruction may be temporary, particularly in cases that have been successfully intubated and have had the electrolyte balance re-established.

## MULTIPLE OBSTRUCTIONS

The diagnosis of multiple obstructions on the plain roentgenogram of the abdomen may be suspected but is exceedingly difficult to substantiate.

The multiple obstructions that one sees may be anything imaginable, but as a rule they fall into several categories: multiple obstructions of the small bowel that are due to adhesions or metastatic cancer (frequently ovarian); those of the small and large bowel caused by tumors (Hodgkin's disease, ovarian neoplasm and so forth); those of the small intestine and colon due to the effects of irradiation; those of the small and large bowel due to an inflammatory lesion (pelvic abscess) or granulomas, such as regional ileitis; those of the colon due to a tumor and an inflammatory process elsewhere, such as diverticulitis.

If the procedure of intubation is employed, the radiologist may frequently make a diagnosis of multiple obstruction on the basis of the following observations. The Miller-Abbott tube may fail to progress beyond a certain point, and gas-distended loops of small intestine may be present beyond the tip of the Miller-Abbott tube; the tube may fail to progress beyond the left lower quadrant, with either gas-distended loops of small intestine distal to the tip of the tube or a distended large bowel, or both; and there may be an obstruction to the barium injected through the tube (with the exception of false ileal obstruction), together with an obstruction demonstrable by a barium enema.

## CAUSE OF OBSTRUCTION

The obstruction is often the final closure of a slowly developing lesion, and such a possibility should be kept in mind. Other causes of obstruction may be many things and conditions, a number of which have already been discussed.

Intussusception may produce strangulation. It is imperative to recognize this condition because a disturbance in the blood supply may be produced without much clinical evidence. This, according to Wangenstein,<sup>1</sup> is due to the sheathing of the gangrenous portion of the bowel by the enveloping walls of the intestine.

If barium can be given by mouth, the nature of the lesion is readily recognized by the large filling defect of the tumor or intussusception, or both, by the narrow lumen of the intestine in the vicinity of the intussusception, except when the intussusception herniates through a gastroenterostomy opening, and by a barium enema, the filling defect of the advancing intussusception in the colon being readily demonstrated. If no opaque mixture is administered, the gas in the loops of intestine proximal to the point of obstruction is readily demonstrated, but when the lesion occurs in infants and children, the observation of gas shadows may be of no assistance, since these shadows are found normally in children up to several years of age. The oblong soft-tissue shadow of the intussusception is also diagnostic.

The roentgenologic observations in strangulated obstructions from other causes are quite different from those just described. One sees tremendous distention of the small intestine when the process involves that organ. In addition, some overdistention of the large bowel may be produced by the peritoneal irritation.

There are a number of conditions that may produce roentgenologic appearances similar to those of a strangulated obstruction. In my experience, some of these have included acute pancreatitis, twisted ovarian cyst, sickle-cell anemia, diabetes, subacute drug (morphine) effects, mesenteric occlusion, ruptured graafian follicle and paralytic ileus. The findings of the clinicians and surgeons must be correlated with the roentgenologic findings before one can make a diagnosis, and, even then, errors will occur.

The question of intubation is being considered more frequently even in those cases in which strangulation is thought to be present. Although the viewpoint of clinicians and surgeons is that only those cases that can be safely delayed should be intubated, I have recently heard conservative surgeons who have had large and successful experiences state that they recommend the passage of

the tube while the patient is being prepared for operation.

### SUMMARY

In a very general way, the roentgenologic signs that might assist in the diagnosis of intestinal obstruction are considered under the following headings: the presence, location, completeness, number and cause.

Some of the experiences with intubation that are of interest to the radiologist are recorded,

particularly those that may lead to errors in diagnosis.

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## INDICATIONS FOR THE USE OF THE MILLER-ABBOTT TUBE\*

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IN a broad sense, the indications for the use of the Miller-Abbott technic of intestinal intubation<sup>1</sup> may be classed as experimental, diagnostic and therapeutic.

### EXPERIMENTAL PROCEDURES

The experimental employment of the method, begun nine years ago at the University of Pennsylvania after two decades of preliminary trial, is worthy of mention because the special clinical applications have always developed from experimental procedures. As a result of the ability to reach any portion of the jejunum, ileum or colon with reasonable ease, the intestinal chemistry, the motor activity of the bowel wall and the responses of the intestine to drugs came under investigation in man. Aspiration of the intestinal contents from chosen regions before and after specific foods has shown the site and rate of absorption, the range of intraintestinal osmotic pressure, the tendency of the chyme to approach neutrality and the mechanisms available to the intestine for maintaining these normal relations. Such data make possible the construction of good jejunal feeding mixtures. By attaching recording instruments to the lumen of the tube leading to the balloon and by injecting radiopaque mixtures locally into the lumen of the intestine, the movements of the intestine and their effects on the behavior of the contents have been determined. The projection of these studies into the clinical field has resulted in the diagnostic procedures to be discussed later. The pharmacologic action of drugs may be investi-

gated from the point of view of secretory, absorptive and motor phenomena in a manner impossible to accomplish in the surgically deranged digestive tract. Thus, from the experience accumulated in hundreds of experimental intubations, the therapeutic methods were developed.

### DIAGNOSTIC PROCEDURES

From these physiologic investigations have come both the diagnostic and the therapeutic procedures dependent on the passage of long tubes. The indications for diagnostic intubation are as follows: suspected absorption defects, such as those that appear to characterize sprue and allied conditions; mild abdominal pain in which the distinction between a neurosis and a small lesion of the intestine is difficult by other means; high-grade obstruction in which it is essential to know the location and nature of the obstructing lesion; and rare conditions, such as gastrointestinal hemorrhage of unknown origin or suspected intravisceral fistulas, when the aspiration of the contents of the intestine reveals the location of a lesion not otherwise detectable.

### Absorption Defects

The claim that a determination of intestinal absorptive power is of diagnostic value is as yet founded on somewhat tenuous evidence. It has long been believed that the group of diseases designated by such names as celiac disease, idiopathic steatorrhea, Gee-Thaysen disease and nontropical sprue is characterized by a loss of the specific absorbing power of the mucosa. The recent work of May and McCreary<sup>2</sup> has cast some doubt on this hypothesis, although the bulk of the evidence to date still supports the older point of view. If one is eventually to demonstrate the validity of

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such a fault as an impediment to the patient's nutrition, one must be equipped with an accurate technic. Attempts have been made to appraise this by determining the blood levels of substances given by mouth. These measures have failed because, obviously, the blood level may be determined as much, or more, by the rate of elimination of the substance from the blood as by the rate of absorption from the intestine. One must then determine absorption by measuring the rate at which the test material leaves the intestinal lumen. Certain methods have been tried in the last few years, such as that of Groen,<sup>3</sup> which depends on the passage of a double-lumened intestinal tube, the distention of a terminal balloon and the retrograde filling of the intestine behind the balloon for a given period. Although this procedure suffices under most normal circumstances, the fact that conditions associated with poor absorption are usually accompanied by bizarre motility changes makes it practically impossible to prevent or to identify technical errors. A disappearance-time technic based on the qualitative testing of intestinal samples for glucose after the ingestion of a stated amount of sugar has been developed by Warren.<sup>4</sup> Noting the time at which the last trace of reducing substance disappears from the chyme gives a measure of the specific power of the epithelium to remove glucose. Although the experimental procedure of Zetzel and Banks<sup>5</sup> is excellent and could be applied as a clinical test, probably the most successful combination of simplicity with accuracy to date is the method of Nicholson.<sup>6</sup> This technic involves the passage of a triple-lumened tube 90 cm. beyond the pylorus, and the institution of a continuous flow of a 10 per cent glucose solution into the duodenum, with continuous aspiration of intestinal contents from a point above an obstructing balloon at the tip of the tube. A known length of intestine is thus continuously perfused with the test solution. The requirements of a good method are that it be simple enough to apply to sick patients, that a unit area of intestinal mucosa be examined, that the application of the glucose solution to the mucous membrane be quick enough to give a sharp starting time, that the residual glucose be removed from the test area at the end of the experiment rapidly enough to give a sharp stopping time, and that the mucosa be constantly supplied with a quantity of the test substance in excess of its maximum absorption capacity yet below a concentration level that would cause mucosal irritation and below a volume level that would grossly flood the intestine. By Nicholson's method, an initial acceleration of the intraduodenal flow can quickly

bring the solution into contact with 90 cm. of bowel, and the final introduction of a magnesium sulfate solution will wash out within two or three minutes the glucose remaining in the test region at the end of the absorption period. Although it is true that the balloon on the end of the tube continues to creep down the intestine at an unknown rate throughout the experiment, so that one ends a half-hour period with more mucosa exposed than at the beginning, the method as a whole is far freer from technical faults than any so far described. If one is to deal accurately with patients exhibiting clinical evidence of absorption defects, a diagnostic method that will unequivocally detect such faults becomes essential.

### *Organic versus Functional Lesions*

The second diagnostic use of intubation is the detection of minimal lesions masquerading as neuroses. This grew out of kymographic studies of intestinal movements. The balloon on the end of a long intestinal tube attached to a suitable recording instrument is a satisfactory apparatus for translating the contractions of the intestinal wall into a continuous graph on moving paper. A localized lesion in the small intestine practically always changes the character of the muscular contractions at that point, producing either local spasm or, if a long-standing partial obstruction has been present, local dilatation. The experience with this method is also too limited to permit dogmatic statements. Since the time for a record may occupy several hours, it may require several years to obtain enough normal control material. Nevertheless, the observations of Ingelfinger and Abbott<sup>7</sup> suggest that, in cases of midabdominal distress with functional symptoms and gastrointestinal x-ray series showing changes of doubtful significance, a balloon record will often tell, first, whether the intestinal disorder is local or general and, secondly, whether, if local, it is spastic or anatomic. From the therapeutic standpoint, this means the differentiation of a lesion possibly correctible by surgical means from one that should best be handled conservatively.

### *Injection of Opaque Mediums for Roentgenoscopy*

A far better established diagnostic use of intubation depends on the injection of an opaque medium.<sup>8-13</sup> This is an important supplement to the kymographic tracing of minimal lesions just described and has drawn the special attention of Boon.<sup>14</sup> A disorder may readily be sufficient to stop the advance of a balloon on a tube while still permitting the advance of a liquid such as a barium suspension. Thus, if during a diagnostic intubation the tube comes to rest at any given

point in the intestine, that region should be carefully examined fluoroscopically and with films during the injection of 50 cc. of a moderately thin water-barium mixture, and again half an hour after the injection, to determine whether the barium has advanced or remained at the point at which it entered the intestine. The fluid flows in the direction of least resistance, and retrograde regurgitation is the factor of chief importance in diagnosing obstruction. Distortion of the lumen, revealed by the advance of barium, may indicate the nature of the obstructing lesion. It should always be borne in mind that local spasm incident to contiguous disease, such as mesenteric lymphadenitis, may simulate a local lesion of the intestinal wall.

A far easier and probably more useful roentgen-ray diagnosis, however, is made by essentially the same procedure, carried out in the presence of complete obstruction. It is obviously unjustifiable to give a barium meal in the presence of a completely blocked intestine. In cases intubated for the relief of distention, it is proper, however, to inject barium down the tube for the detection of the exact site of the obstruction and for the determination of the nature of the lesion. If the block is complete, the injected barium is regurgitated proximally. It is becoming constantly more apparent, however, that decompression of such blockage usually renders the obstruction partial by the relief of local irritability, and improved nutrition aids by reducing the local edema. A little of the barium may therefore be massaged ahead of the tube, and the nature and the extent of the lesion be revealed. It is my opinion that this procedure should be routinely carried out preoperatively in such patients.

#### *Location of Rare Lesions*

Finally, there are those rare conditions whose diagnosis depends on the ingenuity of the physician almost as much as on his previous experience. When a patient bleeds by bowel in the presence of a negative barium enema and of an apparently normal stomach and duodenal cap, the chance of a benign tumor of the small intestine or a Meckel's diverticulum or even a bleeding polyp must be considered. If a tube is advanced continuously down the intestine until blood appears in the drainage, the balloon serves as a signboard to the surgeon, indicating the position of the lesion and making unnecessary the tedious palpation of the bowel that so often results in a stormy convalescence. In similar fashion, a variety of odd clinical circumstances have been clarified by the ability to reach points in the small intestine that were formerly not accessible.

#### Therapeutic Procedures

The therapeutic uses of the long intestinal tube must be considered. Some of these are so specifically surgical as to be out of the province of an internist. One may, however, suggest five chief uses: the prophylaxis against expected intestinal obstruction under unknown or complicated circumstances; the diversion of the intestinal current at a point proximal to the site of an anastomosis, as in surgery of the colon; the decompression of a distended and inactive intestine; the decompression of a distended and obstructed intestine; and the maintenance of nutrition and intestinal function during the course of local peritonitis with obstruction.

#### *Prophylaxis Against Intestinal Obstruction*

Under the head of prophylaxis against intestinal obstruction are included conditions that need only be mentioned, since they are frequently individual problems in themselves. Suffice it to say that in late cases of regional ileitis or in attempts to close traumatic fistulas a surgeon may sometimes anticipate a stormy convalescence before he begins the operation. A tube in the small intestine passed the night before may give him control of a postoperative condition that might otherwise determine a fatal outcome. Similarly, after a total colectomy, edema of the oversewn transverse mesocolon may compress the third part of the duodenum. Death has resulted when this has occurred in conjunction with delayed function of the ileostomy, since gastroduodenal drainage was useless. I now preoperatively intubate all colectomy patients.

#### *Protection of Intestinal Anastomoses and Colon Surgery*

Protection of incised areas of bowel during the postoperative period can be accomplished if a tube lies proximal to the suture line. In the performance of ileocolostomies and one-stage resections of the right side of the colon, much has been said of the importance of preventing colonic distention during the first postoperative days. Probably a more significant, though less obvious, cause of leakage is distention of the ileum proximal to the anastomosis. The patient may show no gross tympanitis because the volume contained within the ileum is relatively small, but for physical reasons the pressures developed are high compared with those in the colon. Thus, a little gas and fluid proximal to an ileocolostomy is far likelier to cause a leak than a large accumulation distal to the suture line.<sup>15</sup> Although decompression of the whole colon, allowing rectosigmoid resection without cecostomy, has occasionally been possible,

the protection of anastomoses is much more valuable.

This is the chief function of the intubation of the small intestine in one-stage resections of right-sided colonic lesions, and although the improvement in mortality statistics — such as 29 cases with 1 death reported by Ravdin and Abbott<sup>16</sup> and 53 cases with 2 deaths recorded by Whipple and Nelson<sup>17</sup> — cannot be attributed solely to the use of the tube, I consider it fair to say that it has been an important contributing factor.

### *Decompression of Paralytic Ileus*

Decompression of simple paralytic ileus, as distinguished from that associated with clinical peritonitis, is worth discussion. I am in complete agreement with Wangenstein<sup>18</sup> that the gas which distends these patients is very largely swallowed air, that the use of the Wangenstein tube for suction often prevents the occurrence of the condition if aspiration is started early enough, and that in mild cases it clears up the condition when once it is established. I disagree with him about the effectiveness of the Wangenstein technic in those cases seen after paralytic ileus has become extreme, with wide distention of the stomach, small intestine and colon, absent audible peristalsis, and the conditions attendant on marked abdominal distention. Whether these cases develop following intraperitoneal procedures or reflexly following injuries or operations on other parts of the body, a tube in the small intestine will progress from region to region, restoring peristaltic activity until the balloon is expelled by rectum. Because of the difficulty in determining when a case is severe enough to warrant intubation of the small intestine rather than the use of the Wangenstein tube, Pitressin, Prostigmine, choline derivatives, irritant enemas, stipes or rectal tubes, it is difficult to appraise the value of this procedure statistically.

Suffice it to say that 29 cases with 6 deaths have been reported by Penberthy, Johnston and Noer,<sup>19</sup> 9 cases with no deaths by Glenn,<sup>20</sup> and 55 cases with 5 deaths by Whipple and Nelson.<sup>17</sup> To these, I add my own experience of 16 cases with 3 deaths.

### *Decompression of Obstructed Intestine*

Decompression of the distention resulting from a mechanically obstructed intestine can be carried out by these tubes with a reduction in the mortality rate. Especially in this group, a careful selection of cases is essential. Suspected gangrene of the intestine, except in certain cases of mesenteric thrombosis, is always a definite contraindication to delaying surgery, and anyone undertaking to use intubation clinically must exert himself to perfect his ability to identify a strangulation. This diagnosis was of somewhat aca-

demic interest in the days when all cases of obstruction were immediately operated on, since the laparotomy promptly revealed the answer. Now that operation may be delayed for days, the patient's survival may depend on whether an impaired blood supply to the involved part is recognized. It is essential to remember that, when one is presented with a case of obstruction, the choice is not between intubation and operation, but between intubation and operation at that particular moment, and on each subsequent visit to the patient's bedside one must re-evaluate the indications for radical or conservative measures. Granting that strangulation is not present, it must be borne in mind that one is intubating for the relief of distention, a condition that, in the absence of strangulation, determines the high mortality in mechanical obstruction. If, therefore, distention does not exist, intubation is not indicated unless some other factor in the case justifies the procedure.

Patients who promptly present colic and hyperperistalsis, and in particular those with conditions giving circumstantial support to the diagnosis of simple obstruction, do not require the passage of a tube. It is in the late cases with marked distention, borborygmi, fecal vomiting, dehydration, electrolyte imbalance and shock — those patients who present on admission the worst surgical risk — that a method of improving the patient's condition before he is operated on becomes most imperative. This is the function of intubation. The tip of the tube advances down the intestine in spite of fecal vomiting until the obstruction is reached. The situation is then under control to such an extent that operation may be delayed for a day or a week or whatever interval is necessary to bring the patient into a sound state of nutritional balance. If the obstruction has not spontaneously subsided, and in certain cases even if this has happened, operation should be carried out.

Justification for this statement lies in the reports of 5 obstruction deaths out of 54 patients by Johnston, Penberthy, Noer and Kenning,<sup>21</sup> of 5 deaths out of 96 patients by Whipple and Nelson,<sup>17</sup> of 3 deaths out of 27 patients by Glenn<sup>20</sup> and of 5 deaths out of 74 patients in my own experience.

### *Relief of Peritonitis with Obstruction*

Finally, intubation enables one to control intestinal function and maintain nutrition in the patient with local peritonitis. Death from rupture of a gangrenous appendix or the spread of a pelvic peritonitis, even after the best surgery, is frequently the result of a combination of two main



factors the peritoneal infection, and the functional blockage of the intestine with uncontrollable distention and the starvation that results. When one controls the obstruction, distention and starvation, the patient, particularly with the aid of sulfonamide drugs, can frequently master his in

of the condition for which the patient is intubated.

Although the technic of intravenous alimentation is a godsend to all of us, it cannot be denied that the number of calories per twenty four hours that can be given by vein is hopelessly inadequate for long time maintenance, and it is frequently

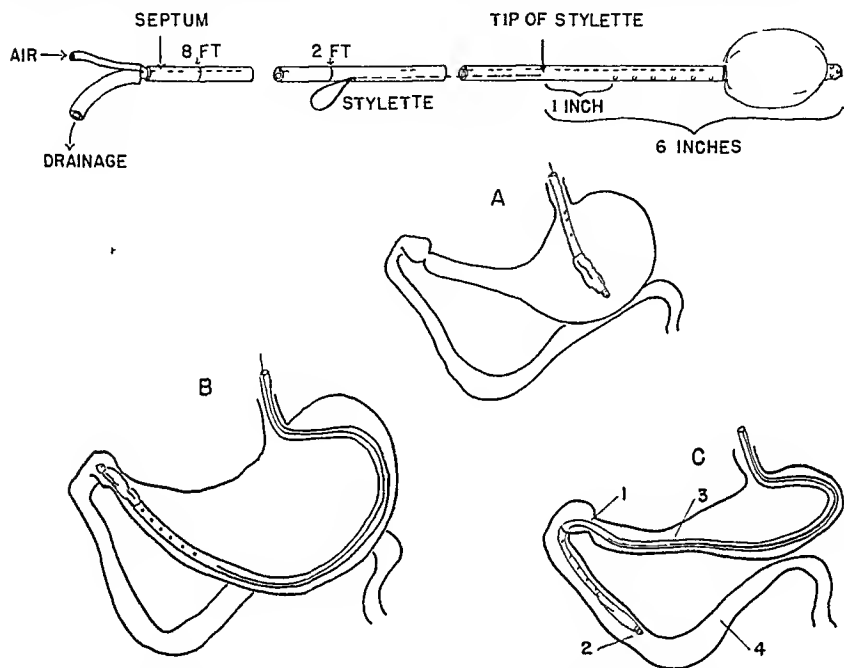


FIGURE 1 Technic of Using a Stylette in Passing a Miller-Abbott Tube

Pierce the wall of the aspirating lumen of the tube at the 50 cm (2 ft) mark with a length of 0.4 mm (0.016 in) diameter, specially straightened, stainless steel vom Hofe leader wire and advance the tip of the wire to a point 2.5 cm (1 in) above the most proximal aspirating hole in the tube. Bend a loop in the other end of the wire so that the tip cannot advance distally. The terminal 15 cm (6 in) of the Miller-Abbott tube will then contain no wire. Pass the tube in the usual manner to the position shown in A. With a temporary adhesive tape patch over the point at which the stylette pierces the tube wall, inject 300 cc of air into the stomach and advance the tube until it lies along the greater curvature, as in B. Hold the tube at the patient's nose to prevent its slipping out, and apply suction to remove the air. The stomach contracts, as in C, squeezing the tip of the tube ahead from position 1 to 2. The tip of the stylette then lies at 1. The antral spasm, with concentric contraction distal to 3, prevents the terminal 15 cm (6 in) from coiling, and the stylette prevents coiling of the tube proximal to the antrum, where the stomach is more flaccid. Draw back the tip of the stylette from 1 to 3, and by gentle, steady pressure on the tube at the nose advance the tip from 2 to 4. Withdraw the stylette, patch the hole through which it was introduced with thin rubber and, having inflated the balloon with 20 cc of air, proceed as usual.

fection. Such obstruction is as a rule self-limited and subsides in from one to three weeks under controlled circumstances. If it is necessary to keep an intestinal tube in place for that long, the question must be asked whether the risk of mucosal erosion by the tube at the larynx or farther down the intestine is greater or less than the danger

unbalanced from the nutritional standpoint. The opportunity given by the presence of the tube to feed a patient 1200 to 1500 calories of low-residue food daily by mouth while the residue is drawn off by the tube is therefore of great advantage. Frequently, after ten days or a fortnight or even longer of complete obstruction, the patient's bowels

begin to move, and intestinal function resumes its normal activity and maintains it after the removal of the tube.

The justification for the use of intubation in cases of this type is based on the report of 24 cases with only 6 deaths by Penberthy and his co-workers,<sup>19</sup> of 8 cases with only 1 death by Glenn,<sup>20</sup> of 92 cases with only 20 deaths by Whipple and Nelson<sup>17</sup> and of my own experience of 27 cases with only 6 deaths.

### TECHNIC

In addition to the indications for intestinal intubation, there remains the question of how to accomplish it. I know of general practitioners who are successfully and judiciously using this method; it is as a rule reserved not only for the hospital but for a physician on the hospital staff who is thoroughly experienced in the many difficulties and minor variations of the technic. If used without strict attention to detail, it is capable of causing great harm, and the interval throughout which one is entitled to persist in attempts to pass a tube rather than in carrying out surgical intervention must be determined in each case individually. This should not be determined by any set number of hours. It has been my own rule, so long as a patient is getting better rather than worse, to wait, irrespective of whether the tube is advancing well or not, but if the patient is getting worse rather than better, I advise operation regardless of what the tube is doing.

Recent developments in the technic have brought the speed of intubation far more directly under the control of the intubator. Following the basic principles laid down by Rousselot and Bauman<sup>22</sup> in 1933 for the use of a stylette in passing duodenal tubes, it has been possible to modify a stylette for use in long intestinal tubes (Fig. 1). With this instrument, one can usually bring the tip of the tube to the duodenojejunal junction within ten to twenty minutes. In a group of 18 severely ill patients with both obstructing peritonitis and mechanical obstruction, failure to accomplish this occurred in only 2. In the remaining 16, it was possible to pass the tip promptly to the distal duodenum, although previous experience had led me to anticipate that many hours would be required to do so. Since a stylette in a gastrointestinal tube is a potentially dangerous instrument, and since it is often far better for the patient if his stomach is thoroughly decompressed before the tip advances to the duodenum, the use of this procedure should not be routine. In the desperately ill patient, however, the ability to decompress the small intestine without delay may be crucial in determining the outcome.

### SUMMARY

Intubation of the small intestine was developed as a technic for studying the physiology of the digestive organs, and from the results have grown diagnostic and therapeutic procedures.

The diagnostic indications for intubation are aimed at the detection of disorders of absorption, minimal lesions ill defined by roentgenoscopy, advanced intestinal obstructions forbidding the use of opaque meals, and rare gastrointestinal disorders unidentifiable by standard methods of study.

The therapeutic indications for intubation are to forestall expected ileus incident to abdominal disease, to safeguard against leakage through intestinal suture lines, to abolish paralytic ileus, to control distention in mechanical obstructions, and to make possible the feeding of patients with peritonitis over long periods while the inflammation is subsiding.

The development of a stylette suitable for use in Miller-Abbott tubes has frequently made possible the prompt passage of the tip into the duodenum under the most adverse circumstances.

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## THE DIAGNOSIS AND MANAGEMENT OF ACUTE OBSTRUCTION OF THE SMALL INTESTINE\*

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IF one excludes strangulated external hernias, the diagnosis of which is easy and the treatment obvious, the diagnosis and management of acute mechanical obstruction of the small intestine remain major problems of clinical surgery. Few questions have stimulated as much experimental work by excellent investigators as, 'What is the cause of death in acute small bowel obstruction?' Although this question has not been completely answered, from the results of these investigations have come certain basic facts that, when considered in the light of clinical experience, suggest a rational scheme for the management of these cases.

The development of such a plan presupposes an understanding of the significant clinical manifestations of the disease and of certain correlated experimental findings, as well as the ability to make a diagnosis.

### CLINICAL TYPES OF OBSTRUCTION

The clinical course of complete obstruction of the small bowel varies greatly, depending on the level of the obstruction and whether or not the obstruction involves the blood supply of the obstructed loop. An understanding of this problem is essential to proper management.

*Simple high obstruction*‡ (duodenal or high jejunal) is usually acute in onset. Vomiting of the juices of the upper gastrointestinal tract is early and profuse. The resulting dehydration is associated with rapid loss of electrolytes, of which the chlorides are the most important. A diminished urinary output and a rise in the nonprotein nitrogen of the blood follow, and there may or may not be an associated alkalosis. Such an obstruction runs a rapid course, in which distention is usually not a major factor, death in most cases results from a loss of essential body fluids. As a rule, early replacement of chloride loss by the parenteral use of physiologic saline solution or 5 per cent glucose in saline postpones or prevents death.

*Low ileal obstruction* is more complicated. The contents of the obstructed loop cannot be emptied

by vomiting. There is some absorption of the electrolytes above the obstructing point, so that the changes in the chemical constituents of the blood are neither rapid nor profound. The accumulation of fluid and gas in the obstructed segment results in increasing distention of the bowel. With the rise in intraluminal pressure, there is slowing of the circulation in the distended segment, congestion and edema of the bowel and, later, injury to the mucosa. It is probable that absorption into circulation ceases when the intraluminal pressure is sufficiently high. A replacement of chlorides in these patients does not materially influence the usual course of the obstruction. Some other factor or factors are responsible for death in these cases.

*Strangulation obstruction*, due to constriction of the mesentery of a loop of bowel and resulting in interference with its blood supply, regardless of the level of bowel involved, is a rapidly fatal condition, unless the constricting band is divided before irreversible changes take place in the bowel, or unless the devitalized bowel is removed from the peritoneal cavity. Death may occur from shock before development of the peritonitis that follows permeation of the devitalized bowel by intestinal organisms.

### DIAGNOSIS

The old teaching, 'Any patient with an abdominal scar and an attack of abdominal pain has an acute small bowel obstruction until proved otherwise,' should not be allowed to jeopardize those patients who have never been operated on but in whom such a condition may arise. Approximately 20 per cent of the patients seen at the Massachusetts General Hospital have had no previous operation.

The five important diagnostic criteria are as follows:

*Pain*, sudden in onset, severe and colicky in nature, usually at or above the level of the umbilicus but at times in the lower abdomen or generalized, is the presenting symptom in nearly every case of acute small bowel obstruction. This pain may be constant if strangulation is present or in the later stages of a simple obstruction. It may even disappear late in the course of the disease.

\*Presented at the annual meeting of the Massachusetts Medical Society on May 1, 1941.

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‡Simple obstruction means occlusion of the lumen of the bowel without interference with its blood supply.

*Vomiting* follows the pain. It may be small in amount or, in the later stages, copious and fecal in character. The so-called "fecal vomiting" frequently associated with intestinal obstruction is usually a late symptom and of no great help in an early diagnosis.

*Hyperactive, tinkling, high-pitched peristalsis*, audible over the abdomen, is often present, and although it is not necessary for a diagnosis, its presence is highly suggestive.

*X-ray evidence of one or more distended loops of small bowel*, as shown by a scout film of the abdomen, is the most useful single objective finding in a patient with small-bowel obstruction. The x-ray film should be taken after the stomach has been emptied of its fluid and gas content, and before an enema has been given. This avoids the confusing factors of gas and fluid in the stomach and the possible error due to the instillation of gas and fluid into the colon and its subsequent incomplete evacuation. I have observed dilatation of coils three hours after the onset of pain. On the other hand, I have seen two proved cases of obstruction during the past year (one with strangulation and the other a simple obstruction) in which there were no abnormal gas shadows. The inexperienced should be warned that the interpretation of existing shadows may be difficult. The small bowel may be so dilated that an x-ray diagnosis of large-bowel obstruction is made. In some cases in which the interpretation of gas shadows has been difficult, positive identification of the colon by injection of a small amount of barium by rectum has proved most helpful, and from this maneuver there have been no ill effects. In other cases, a repeat film after six hours may show a change in size or distribution of the gas which will facilitate a more accurate diagnosis.

*Constipation.* Characteristically, there is cessation of the passage of gas or feces by rectum following the initial pain. Small amounts of gas or feces may be passed, however, since in many cases the bowel below the obstruction empties itself of its contents. Moreover, the obstruction may at first be incomplete, and small quantities of gas may pass into the lower segment. Abdominal cramps with hyperactive peristalsis and little or no gas passing by rectum are strongly suggestive of an obstruction at some point in the intestinal tract.

*Strangulation obstruction.* When the diagnosis of small-bowel obstruction has been suspected or made, a more detailed interpretation of whether the obstruction does or does not interfere with

the blood supply to the obstructed loop is of the greatest advantage. In my experience, such a differentiation can readily be made in the later stages of the process, but only rarely in the early hours of the disease. Gangrene may develop very rapidly, as in a patient operated on six hours after the onset of symptoms and requiring resection of a gangrenous segment of bowel.

The pain in strangulation obstruction is usually steady, with or without associated spasms of colic. I have treated several patients with strangulation obstruction who complained of pain in the mid-back, a symptom not commonly encountered in the absence of interference with the mesenteric structures. Although tenderness may be present over the constricting point in simple obstruction, any increase or spread of this tenderness should be interpreted as evidence of strangulation, particularly if the tenderness is associated with muscle spasm. The leukocytic count is too uncertain to be of value. An abdominal tap is easily and safely done, and may prove useful in doubtful cases. A small-gauge hypodermic needle of adequate length or a 20-gauge or 22-gauge lumbar-puncture needle is used. The finding of blood-tinged fluid warrants a diagnosis of strangulation obstruction. A negative tap does not exclude it, however.

The diagnosis of strangulation obstruction is difficult to make early and costly to make late; it is therefore safer to operate promptly on all patients seen in the first twenty-four hours of their attack, since during this period, gangrene—whether incipient or actual—can usually be cured.

#### CAUSES OF DEATH

*Experimental.* Any attempt to review the experiences of the laboratories in the effort to determine the presence or absence of a toxic factor in death from simple obstruction of the small bowel would only confuse the clinician. However, from these laboratories have come many valuable facts that are accepted by most workers and are essential to an understanding of the treatment of these conditions. They may be briefly summarized as follows:

In simple high intestinal obstruction, death comes as the result of dehydration and chemical imbalance from loss of the juices of the upper gastrointestinal tract, whose replacement with physiologic saline solution prevents or greatly postpones a fatal outcome.

In simple low obstruction, other factors are involved, since replacement therapy does not greatly alter the length of life of such animals.

Distention is a constant and essential factor in the fatal cases without gangrene.

Distention is due primarily to gas—most of which is swallowed air—and intestinal fluid. Associated with or secondary to distention are marked increase in the bacterial count of the bowel content, diminution of the circulating plasma and blood volume, and slowing of the circulation in the bowel wall, with consequent interference with absorption and, later, injury to the mucosa.

Strangulation obstruction is associated with rapid and marked diminution of the circulating plasma and blood volume, and early injury to the bowel wall, with increased permeability to bacteria and ensuing peritonitis. Death follows in most cases from the effects of strangulation rather than as a result of the associated obstruction.

The dictum of the laboratories, therefore, is clear: lost chlorides should be replaced, distention should be relieved or prevented and in strangulation obstruction, lost plasma and blood should be replaced. If once, the strangulating mechanism should be relieved, and the necrotic bowel should be removed.

**Clinical** Whatever the lethal factors in experimentally produced obstruction may be, the fact

TABLE 1 Causes of Death in Acute Small Bowel Obstruction at the Massachusetts General Hospital 1924-1941

CAUSE OF DEATH	NO. OF CASES
Peritonitis	1
Pulmonary collapse or pneumonia	2
Shock	4
Miscellaneous	3
Total	9

remains that 29 patients dying from acute small bowel obstruction at the Massachusetts General Hospital in the last seventeen years may be readily grouped under four different headings (Table 1).

All but 4 of these patients were operated on. In 3 (all with strangulation), the diagnosis was made at autopsy, and the fourth patient died of aspiration of vomitus during passage of a stomach tube. Eighteen of the 29 deaths were secondary to strangulation obstruction.

Not satisfactorily explained, either in the laboratory or from the hospital records, is the sudden collapse, usually fatal, that is occasionally seen following operation and the sudden release of a distended obstructed bowel either into the lower segment or externally.<sup>1</sup> Whatever its cause, it is a clinical entity that cannot be overlooked in the management of the distended bowel.

In a recent analytical study of 136 cases at the Massachusetts General Hospital,<sup>2</sup> certain pertinent clinical facts were re-emphasized.

Following the teaching that early diagnosis and operation are indicated on patients who are good risks, and relief of distention by simple blind ileostomy without exploration on those who are poor risks, the mortality in simple obstruction over a ten year period has been reduced from 31 to 12 per cent.\*

In 42 patients seen and operated on within twenty four hours after the onset of symptoms, there were no deaths, whereas in 17 patients entering within this period whose operations were delayed into the second twenty four hours,† 5 (29 per cent) died.

Fourteen (64 per cent) of 22 patients sixty years of age or older, and 6 (75 per cent) of 8 patients seventy years of age or more, died following operation.

Careful insertion of a No. 16 or 18 Fr catheter into a loop of distended bowel, using the Witzel or a comparable technic, without exploration of the abdomen, was a lifesaving procedure in late cases with marked distention. On the other hand, this same procedure in association with any attempt at exploration or manipulation of the bowel ended fatally, usually from peritonitis, in most patients so treated.

Thus, from a study of these records of patients, living and dead, it is apparent that prompt hospitalization, early diagnosis and early operation give good results, and that late diagnosis and early operation on a highly infected, distended or gangrenous bowel give poor results.

#### TREATMENT

From a knowledge of the foregoing experimental and clinical facts, the ideal treatment for acute intestinal obstruction can be readily formulated. In addition to prompt diagnosis and early operation (two or three hours after hospital admission) on all patients seen within twenty four hours of the onset of symptoms, immediate operation on any patient with strangulation obstruction should be performed. Substitution therapy, consisting in glucose in physiologic saline solution sufficient to restore lost electrolytes, should be instituted promptly. Prompt transfusion with plasma or whole blood into patients with marked distention or strangulation obstruction is indicated.

\*The increase in use of the early nasogastric tube and Wargens rectal suction undoubtedly contributed greatly to these results.

†Delay in these patients was due to inability to make a diagnosis of obstruction or because the condition was not considered as likely serious enough to warrant immediate operation.

Evacuation of the obstructed segment, to release distention, should be carried out before one attempts to relieve the obstructing factor in patients, seen twenty-four hours or more after the onset of symptoms, who have distended bowel on physical or x-ray examination.

The pioneer work of Wangenstein<sup>3</sup> on suction drainage of the upper gastrointestinal tract, given a new impetus by Miller and Abbott<sup>4</sup> and Johnson and his associates<sup>5</sup> by the demonstration of a practical method of draining the lower segments of the small bowel, has overcome the one difficulty—the relief of distended bowel in the patient with a simple but otherwise fatal obstructing lesion—in the application of the above principles to clinical medicine.

In November, 1939, the Committee on Small-Bowel Obstruction was organized at the Massachusetts General Hospital for the supervision and study of all such cases entering the hospital. This committee consisted of Dr. Richard Warren, the current residents on the two surgical services and myself. The actual treatment of the patients was carried out by the men on duty, as in the past.

Based on the principles outlined above, the following recommendations (previously expressed by two of the committee<sup>2</sup>) were given a trial:

Prompt replacement therapy is instituted for all cases and is continued according to the degree of chemical or fluid imbalance.

A double-lumened Miller-Abbott tube is passed immediately, and the stomach emptied of its fluid and gas contents. The patient is sent to the X-ray Department for a scout film, and an attempt is made to pass the tube through the pylorus at that time if evidence of small-bowel obstruction is present. If operation is to be done, suction is applied and maintained throughout the procedure to prevent regurgitation and possible inhalation of intestinal contents.

Operation is performed two or three hours after admission on all patients seen within the first twenty-four hours\* of the onset of symptoms, and on all patients with a diagnosis of strangulation.

Operation within six to eight hours is carried out in most cases seen in the second twenty-four hours after the onset of symptoms, except in patients sixty years of age or older and in those with marked distention.

Nonsurgical drainage is instituted for all patients sixty years of age or over who enter the

hospital twenty-four hours or more after the onset of symptoms, and in all patients whose symptoms are forty-eight hours† or more in duration.

If intubation is unsuccessful, if the patient is not relieved by continued aspiration of the stomach over a period of six to eight hours, if the degree of distention clinically or by x-ray study is not excessive, and if the patient is in good surgical condition, immediate laparotomy under general or spinal anesthesia should be performed.

If intubation is unsuccessful and if the age or condition of the patient or the degree of distention makes release of the obstruction hazardous, a blind enterostomy is done under local anesthesia. A catheter (No. 16 to 18 Fr.) is placed into a distended loop of bowel with aseptic technic and without exploration. If bloody fluid is found, the loop of gangrenous bowel must be found and delivered from the abdomen, regardless of the condition of the patient.

In good-risk patients, an operation of election should be done in those cases that have been successfully decompressed, regardless of whether the mechanism of obstruction has been outlined by the instillation of barium through the tube.

#### RESULTS OF TREATMENT

During the last eighteen months, 29 patients have been seen and followed by this committee. A correct diagnosis of strangulation was made once. It was not made but was present in 3 cases. Seven cases are excluded from this study because they were secondary to a carcinomatosis, pelvic infection or other conditions in which obstruction was only a contributory factor. Twenty-two cases of the type under discussion were seen. The number is too small to permit more than a report of progress, but these cases have been carefully studied, followed and reviewed at frequent committee conferences, and have been helpful in guiding us in the continued care of these patients.

*Diagnosis.* A correct diagnosis was made in 20 cases. Improper interpretation of scout films resulted in an incorrect diagnosis of large-bowel obstruction in 1 case, and 1 patient died of an undiagnosed strangulation.

Positive x-ray findings were present in all but 2 cases. The films in one of the positive cases were misinterpreted, and in another, an incorrect

\*The time limits set are of necessity somewhat elastic, but have proved to be of greatest help in deciding for or against early operation. It is only within the first twenty-four hours of the attack that most patients with strangulation can be saved, and that practically all patients with a simple obstruction can be safely operated on.

†Theoretically, all patients with simple obstruction not moribund on admission and without some serious constitutional disease should survive if properly treated. This is not so with strangulation obstruction unless the patient is operated on before irreversible changes have taken place (usually within twenty-four hours). After twenty-four hours have elapsed, 70 per cent of our patients with strangulation have required resection, with a mortality of 70 per cent. It is therefore safer to accept the hazard of strangulation than the risk of operation on the distended patient with a simple obstruction.

interpretation was made during the night by the Surgical Service and the roentgenologist on call, to be corrected the following morning by one of the senior members of the X ray Department. There is no question that the correct interpretation of these films is at times very difficult, but it is equally striking that without the use of a scout film the diagnosis could not and would not have been made in some of these patients. The 2 cases with no evidence of abnormal gas shadows are also of importance in indicating that negative x ray study must not be construed to exclude a diagnosis of acute obstruction.

**Miller-Abbott tube** A Miller-Abbott tube was passed in all patients but 2 infants with intussusception. As soon as the diagnosis was made, an effort was made with the fluoroscope to place the tube at or to pass it through the pylorus. In 10 of 20 cases, it did not pass the pylorus, owing in 3 cases to early operation, in 1 to spontaneous release of the obstruction, and in the 6 others to technical inability to get it through\*. It should be emphasized, however, that all these patients are benefited by the continuous aspiration of the stomach. I should probably be embarrassed to admit such a high percentage of failures, if I did not know that failure resulted only after a sincere effort by men of experience equal to that which I believe to be available in most well-organized hospitals. Because of this, 2 blind ileostomies were carried out successfully, one before and one after operation. Because of the difficulty of intubation, I believe that much valuable time may, but need not, be lost in prolonged unsuccessful attempts to obtain passage of the tube. This is particularly true in the earlier stages of the obstruction, when a corrective operative procedure can frequently be safely carried out.

**Mortality.** All but 1 of these patients were operated on, the exception being a seventy-two-year-old woman who responded well to suction drainage and whose age made elective operation inadvisable. There were no deaths from simple obstruction in this group of patients, although in 2 patients, both over sixty years of age, a note is made in the record that decompression by means of the Miller-Abbott tube (extending in one case for five days and in the other for eleven days) was life-saving. From a review of these cases, it is quite likely that had early operation been instituted, as the custom has been in recent years, death would probably have resulted in each case. Interestingly enough, were this so, the mortality in this small group would be the same as that for simple ob-

struction in the last decade at the Massachusetts General Hospital.

There were 4 patients with strangulation obstruction, 2 of whom died. One of them was a man of sixty-seven who entered the hospital acutely ill twenty-four hours after the onset of symptoms, on whom operation under local anesthesia was done in an attempt to save his life after all other efforts to improve his condition had failed. The second death was in an eighty-year-old woman who entered the hospital only seven hours after the onset of symptoms, who was followed for twenty-three hours after admission, whose x ray films showed no abnormal gas shadows, and who was finally operated on without a positive diagnosis, a strangulation obstruction requiring resection being found.

### SUMMARY

The important experimental and clinical evidence affecting the treatment of acute obstruction of the small intestine is summarized.

A working plan for the management of these cases is presented, and the results in a small group of 22 cases are reviewed. There were 18 cases of simple obstruction, with no deaths, and 4 cases of strangulation obstruction, with 2 deaths.

The value of early hospitalization and early operation in patients seen within twenty-four hours of the onset of symptoms is again emphasized.

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\*In recent months the use of a fine stylette, as suggested by Abbott<sup>4</sup> has greatly facilitated intubation in cases in which difficulty has been encountered.

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## THE TREATMENT OF TETANUS\*

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THE treatment and nursing care of a patient severely ill with tetanus present a difficult medical problem. When we were faced with such an emergency, we turned to the literature for guidance but were disappointed by finding no adequate description of the clinical course of such a patient. Because of this apparent lack, we offer the following case report in detail, hoping that it may lend courage and help to those engaged in caring for patients with severe tetanus.

### CASE REPORT

B. M. (M. G. H. 258145), a 10-year-old boy, was running on the ocean beach on June 29, 1940, when he struck the side of his left foot at the base of the small toe. At first, this was thought to be a stone bruise, but the next day it was found that a splinter had penetrated the skin. The splinter was removed, and iodine applied; 3 days later he visited his family doctor, who advised hot boric soaks. By July 3, the area showed signs of inflammation and yielded a small amount of pus. The patient occasionally soaked the foot as advised but was active in play until July 5, when he did not feel well and complained of a backache at evening and passed a restless night. On the morning of July 6, he complained of headache, backache and a stiff neck. When seen at home at 11 a.m., he was in typical tetanus, with opisthotonos and risus sardonicus, and he had severe muscular spasms when touched. He was given phenobarbital and ½ gr. morphine, and transferred to the Massachusetts General Hospital at 1 p.m.

Sedation was started with 3 gr. sodium luminal subcutaneously, and at 2 p.m., under ether anesthesia, the area about the base of the little toe was excised and two black splinters of wood were removed. Cultures of these splinters, the longest 1 cm., yielded *Clostridium tetani*. An intracutaneous test with horse serum was negative. Although the patient's older brother was a known asthmatic, it was decided to give horse-serum tetanus antitoxin. He received 20,000 units of antitoxin about the wound, 20,000 units encircled about the left mid thigh and 20,000

units in an intravenous injection of 5 per cent glucose in physiologic saline solution. At 4 p.m., another 40,000 units of antitoxin was added to the fluid being given intravenously. A lumbar puncture was performed, and the fluid removed was replaced by an equal amount of fluid containing 10,000 units of antitoxin.

The patient remained under fair sedation, with a total dose of 12 gr. of sodium luminal subcutaneously and ½ gr. morphine in the first 12 hours. The back was arched, and he had intermittent, severe muscular spasms throughout the night.

A lumbar puncture at 10 a.m. on July 7 showed an initial spinal-fluid pressure equivalent to 400 mm. of water, which was reduced to 200 mm. by removing an opalescent fluid containing 1350 polymorphonuclear leukocytes per cubic millimeter; 50,000 units of antitoxin was given intravenously at 10 a.m., another 20,000 units at noon, and another 20,000 units at 3 p.m. The first severe convulsion came at 5 p.m.; fortunately, the resident physician was in the room and administered ether anesthesia and adrenalin. Several convulsions followed, and at 10 p.m. another lumbar puncture was done; again the initial pressure was 400 mm. and was reduced to 100 mm. by drainage of spinal fluid. An additional 10,000 units of antitoxin was given intravenously at 11 p.m. During the night, there were convulsions every 15 to 30 minutes, and the nurse administered ether and frequently aspirated the nose and the throat through the airway tube, which had been inserted at the time of the first convulsion. In this 24-hour period, the patient received 27 gr. of sodium luminal subcutaneously and also 7½ gr. of Sodium Amytal. Dressings of the foot wound with powdered sulfapyridine were done twice daily.

A severe convulsion at 7 a.m. on July 8 led to intense cyanosis, and oxygen, flowing at a rate of 4 liters per minute, was accordingly made available through a tube passed into the ether cone. At 8 a.m., another lumbar puncture was done, and the pressure was reduced from 350 to 100 mm. This definitely relieved the patient. Because of the sustained fever, the nurses—two special nurses worked together—applied to the trunk and extremities towels wrung out in cold alcohol; usually, 20 minutes of such application was sufficient to cause a drop of at least 2°F. in temperature. Throughout the day, his condition was poor, the respiratory rate and pulse increasing. At 4 p.m., convulsions began after an attempt to catheterize a very full bladder. The cyanosis and la-

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bored respiration were helped by intravenous adrenalin, which was stopped when the pulse became rapid and feeble. At 9 p.m., a severe convulsion caused respiration to cease for 3 minutes. A lumbar puncture was done at 10 p.m., and the spinal fluid pressure was lowered from 300 to 75 mm., with definite relief. Ice packs were applied to the head at this time, and the patient seemed improved by these measures. In these 24 hours, he received 18 gr of sodium luminal subcutaneously—much of it at the discretion of the nurses.

On July 9, convulsions of moderate intensity continued about two in each hour, until 9 a.m., when another lumbar puncture was performed with considerable difficulty owing to the marked degree of opisthotonos. The intral pressure was found to be lower—250 mm. After drainage, with reduction of the pressure to 100 mm. the patient seemed easier, but respirations were rapid and considerable mucus in the air passages and in the airway led to the use of 1/100 gr of atropine subcutaneously in repeated doses. Because of the cyanosis and rather feeble and shallow respirations, all sedation was omitted. By afternoon, the patient seemed better, although edema of the extremities had appeared. By 8 p.m., respirations were stronger, and he occasionally sighed heavily. Cold packs were again administered, and there was a drop of 2°F in temperature.

Throughout the morning of the next day, the patient began to come out from under the previous sedation and convulsions returned in rapid succession. Cyanosis, labored respirations, made noisy by secretions in the bronchi and a pulse that was too rapid to count made us believe that he was in a very critical state. Sodium Amytal, 3½ gr every 3 hours, was resumed, and a transfusion of 500 cc of citrated blood was given slowly. Edema persisted and interfered with venipunctures. By evening, the patient was quieting down and seemed further improved after a lumbar puncture and drainage at 10 p.m., but an attempted intravenous injection again precipitated a severe convulsion. The total medication in these 24 hours was 22½ gr Sodium Amytal and 1/75 gr atropine.

On July 11, the convulsions lessened in duration and intensity during the day, and for the first time the nurses did not administer ether during the seizures. At noon the patient slept for 2 hours, and after this he passed gas and voided. Later, there were three convulsions that required the administration of ether. Edema continued so that 1000 cc of 5 per cent glucose in distilled water was given intravenously. Up to 9 p.m., 22½ gr Sodium Amytal and 1/100 gr atropine were given.

No sedative was given on July 12 until the patient suddenly had a severe convulsion at 8 a.m. This required ether. Several muscle spasms continued, and at 2 p.m. a lumbar puncture was done again and the pressure lowered from 200 to 75 mm., with immediate and striking improvement. No food or fluids had been taken by mouth up to this time, and at 10 p.m. the patient was therefore etherized and a nasal catheter passed through the left nostril into the stomach, hourly feedings of 45 cc of an equal mixture of milk and lime water were begun. Acidosis was suspected, but we were hesitant to find that the blood chloride was 99 milliequiv per liter (normal, 100 to 105 milliequiv), and the carbon dioxide combining power 24.3 vol per cent. The nonprotein nitrogen was 27 mg per 100 cc, the red-cell count 4,630,000 and the hemoglobin 15.6 gm. Throughout this day, the edema subsided, and the patient received 18½ gr Sodium Amytal and 6 gr sodium luminal after 8 a.m.

The next day was encouraging, since there were only

a few severe convulsions, and by evening there were only short spasms of the back, chest and leg muscles. The large amount of mucus in the throat and airway forced us to continue the use of frequent suction of the upper air passages and the repeated use of atropine. The total intake of milk and lime water by gavage was 1480 cc. Sedation totaled 11 gr of sodium luminal and 1¼ gr of Sodium Amytal.

On July 14, the patient seemed quieter until 5 a.m., when he vomited, became cyanotic and had a severe convulsion. The nurse then noted a diffuse, dull reddish, morbilliform eruption. The fever and respiratory rate increased, and the pulse could not be felt. The jaws were still tightly locked, and the body was becoming cyanotic. The situation was precarious and we feared that the patient would not survive the shock of serum sickness. At 11 a.m., we finally succeeded in completing a lumbar puncture, but we were surprised to find a normal intral pressure—150 mm. The only treatment through this period was continuous oxygen by nasal etherizer and repeated cold packs to the entire body. An intravenous injection of 500 cc of 5 per cent glucose in distilled water was given in the hope of preventing edema. Feedings of milk and lime water through the nasal tube were continued. Sedation in this 24 hour period was 11 gr sodium luminal and 7½ gr Sodium Amytal.

On July 15, the worst seemed over and by 3 a.m. the pulse was palpable. Cyanosis continued throughout the day, and the pulse became very thready in the afternoon, we therefore decided to transfuse him, 300 cc of whole blood plus 150 cc of saline being given. By 10 p.m., the patient looked better and breathed more easily, and the pulse was of better quality. A bloody nasal discharge began, and the nasal oxygen catheter was removed. He seemed weak and tired, and this was the first day without convulsions—there were only spasms of the muscle groups. The total sedation in these 24 hours was 12 gr sodium luminal and 3¼ Sodium Amytal.

On the following day, the nurses were encouraged, and for the first time admitted that the patient might recover. He was noisy, cried out, and had an excessive amount of bloody mucus in the upper air passages. There were no spasms from 3 until 10 p.m. A high-calorie feeding mixture was started, and he was given 30 gr chloral hydrate twice through the feeding tube. In this period only 3 gr of sodium luminal was given.

On July 17, the patient continued to groan and have muscle spasms, and the teeth could be separated about 10 cm. Frequent aspiration of the upper air passages was still necessary because of excessive mucus secretions. He was controlled with two 15 gr doses of chloral hydrate through the feeding tube and 30 gr once by rectum.

On July 18, fever and a bloody nasal discharge about the feeding tube, which had been in place for 6 days, caused some concern. It was removed, and careful aspiration, followed by argyrol in the nose, preceded its reinsertion through the right nostril. A furuncle appeared on the left shoulder, so that the patient was turned every hour. Throughout the day, he was restless, the eyes moved, and he cried out at 9 p.m., he first answered. Yes and squeezed the nurse's hand. The nasal tube was removed at 5 p.m., and from then until August 2 it was put down each morning for the gavage feedings throughout the day and removed about 9 p.m.

The patient continued to have spasms about every two or three hours on July 19, but he was slowly gaining consciousness and voided in the urine. He perspired freely, and mild dehydration was balanced with an intra

venous injection of 800 cc. of 5 per cent glucose in saline. The sedation in these 24 hours totaled 5 gr. of sodium luminal and 30 gr. of chloral hydrate by rectum.

On July 20, the condition was about the same, and the patient was trying to talk. Much mucus secretion was aspirated from the upper air passages. An abscess on the scalp was noted. The sedation was 12 gr. sodium luminal.

From July 21 to August 1, the chief problem was a sudden, rapidly spreading furunculosis and cellulitis of the head and neck. The scalp was shaved, individual abscesses were drained, and alcohol and iodine were applied thrice daily. This treatment was painful but effective, although a large cervical abscess had to be drained under ether anesthesia on July 28. Likewise, pressure areas on the shoulders and back demanded constant nursing attention. The amount of feeding by tube was gradually increased, and the patient tolerated high-calorie mixtures, orange juice and 20 mg. of vitamin B daily. On July 24 and again on July 30, a loose tooth was discovered and removed. On July 24, some concern was caused by signs of congestion in the right upper lung, and an x-ray film of the chest disclosed a small dense area in this region. This, however, rapidly cleared, and on July 30 the chest film was normal. There was no evidence of a fracture of the ribs or vertebrae. By July 27, the patient was able to swallow sips of water, but tube feeding had to be continued. From July 25 to 31, he was often disorientated, screaming and having hallucinations. Spasms of the muscles continued to keep the back arched, and we were unable to extend the legs completely. The sedation used in this period was chiefly sodium luminal subcutaneously, usually 3 to 6 gr. at night.

August 1 to August 29 marked the true period of convalescence in which each day showed a little gain in the general condition. August 2 was the first day in which the patient swallowed small amounts of soft food and could speak clearly but slowly. By August 5, he enjoyed having a book read to him for a short time. On August 6, another cervical abscess was drained, and on that day he listened to the radio and also fed himself.

On August 7, the red-cell count was 4,330,000, and the white-cell count 10,100. By August 14, the red-cell count had dropped to 4,000,000, and 4 gr. ferrous sulfate was given twice a day. On August 19, the first hour in a wheel chair caused a marked response, with fever, elevation of the pulse and fatigue. A swollen right axillary node began to cause pain and increased in size despite local applications of heat; on August 22, it was incised and drained. On August 27, the patient received 1.0 cc. of tetanus toxoid subcutaneously. After this, improvement was rapid, and he was discharged home on August 29.

On December 3, he was seen in the office and was given a second injection of 1.0 cc. of tetanus toxoid. At this time, he appeared entirely healthy and was mentally alert. He returned to school on January 6, 1941.

### DISCUSSION

Several features of this case warrant emphasis. The first is that the original injury occurred on the beach, an unlikely place for tetanus bacilli; one of us (R. H. M.)<sup>1</sup> had previously written that "ordinary wounds acquired in the home or in clean places, free from possible fecal contamination, or while bathing at the shore should not

require tetanus antitoxin." Obviously, we can no longer regard the seashore as safe from tetanus infection. As Moore and Singleton<sup>2</sup> have recently pointed out, this disease is present all over the United States, but its geographical distribution is highest in the South and least in New England. Despite this reassurance to those in the cooler climates, it is known that tetanus causes over a thousand deaths yearly in this country.

The second feature is that the onset of tetanus six days after the injury indicated a poor outlook. The direct relation between the incubation period and the mortality in this disease has been known since the time of Hippocrates, but the recent statistics of Kirtley<sup>3</sup> are of interest. He found that 72 per cent of those developing tetanus within ten days of the injury died in one to sixteen days; death followed in only 18 per cent of those developing it ten days or more after the injury. The short incubation period in our case is indicated in Figure 1.

In the treatment of this case, we employed six principles that we believe were of almost equal value in restoring this boy to health: profound sedation, surgical removal of the focus of tetanus, moderate intravenous dosages of tetanus antitoxin, frequent lumbar punctures, maintenance of adequate respiratory exchange and the most intelligent nursing care.

Adequate sedation is of utmost importance, and we agree with Spaeth<sup>4</sup> that enough sedation to relax the patient should be given before operating to remove the focus of tetanus bacilli. In this way, one avoids precipitating severe and possibly fatal convulsions early in the disease. The sedatives that we chose were sodium luminal, Amytal and chloral hydrate in large doses, but Evipal, Pentobarbital and others are probably equally effective. We believe that morphine and other respiratory depressants are contraindicated because death may occur from respiratory embarrassment. Likewise, we cannot recommend avertin, magnesium sulfate, paraldehyde or other drugs known to cause occasional constitutional reactions. Curare and similar substances are not yet generally available, although the use of curare has been reported by Cole<sup>5</sup>; evidently, its therapeutic and toxic levels are dangerously close to each other.

The second principle is the need for the complete surgical removal of the focus of infection, which can best be done under general anesthesia. The wound should be left open and allowed to heal from the bottom. The topical use of sulfa-pyridine or another sulfonamide is probably of value in sterilizing the wound.

A most encouraging and instructive experience comes from Africa, where Bryant and Fairman<sup>6</sup> observed that the natives demanding the same treatment for tetanus as for cerebrospinal meningitis were given lumbar punctures and enough Evipal to keep them anesthetized for three or four days. In these cases, tetanus antitoxin was never given, whereas in some of the later cases

It occurs to us that such a procedure should also delay the onset of serum sickness until the patient is better able to withstand it. In treating children, Dietrich<sup>7</sup> urges a slow but safe way to give serum antitoxin—the intramuscular route. Although our patient received an intrathecal injection of 10,000 units of antitoxin, it was done against the advice of one of us (R.H.M.). Since

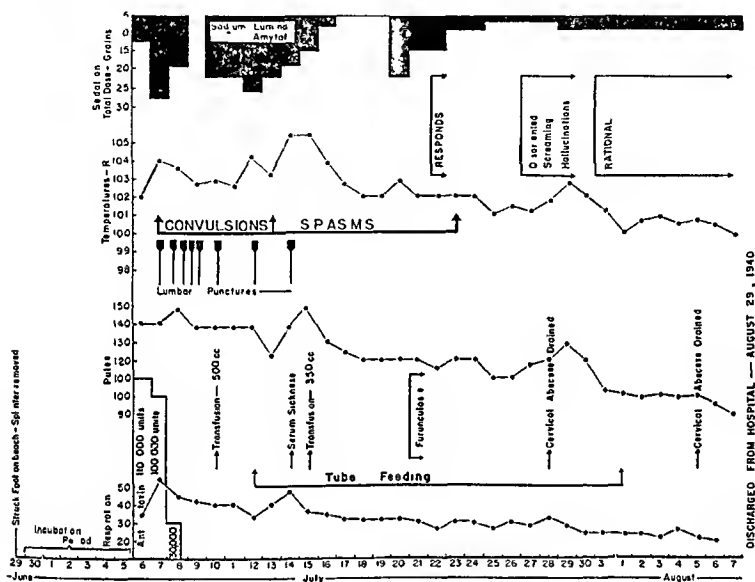


FIGURE 1 Diagrammatic Summary of Data.

sulfapyridine was administered. Unexpected recoveries were made under this therapy, and in the last 22 cases so treated only 5 patients died, which is a lower mortality than most reported series from this country.

This experience of Bryant and Fairman throws into sharp relief the problem of whether to give antitoxin, and if so, by what route it should be given and the optimum amount to give. We advocate a moderate dose of the wound and intravenously with physiologic saline for the first few days of the disease. It seems unnecessary to give enormous doses, for it has been shown experimentally that if one full lethal dose has reached the spinal cord, a million neutralizing units of antitoxin do not save the animal.<sup>7</sup> The daily injection of 5000 units of antitoxin has been recommended by Firor<sup>8</sup> to ensure the maintenance of an adequate titer of antibody in the blood stream.

then, the reasons summarized by Hall<sup>10</sup> make this route seem quite inadvisable.

The next principle, possibly the most important one in our treatment, was the frequent drainage of spinal fluid. This procedure seems not to have been emphasized in previous reports. It is known that the cerebrospinal fluid is under an increased pressure during profound sedation and also during convulsive seizures; we therefore reasoned that lumbar puncture might bring relief to a patient in severe tetanus. The prompt alleviation afforded by these procedures seemed mechanical, allaying the nervous tension and convulsions.

The maintenance of a clear airway, an adequate supply of oxygen, the control of bronchial secretions and other measures such as the care of the skin, frequent turning, careful feeding by tube and the many details of the sickroom were largely the responsibility of the nurses.

Finally, we wish to direct particular attention to the use of tetanus toxoid. This should be used not only as a part of routine immunization in childhood but also at the time of injuries suspected of introducing tetanus bacilli. The occurrence of tetanus after the usual prophylactic dose of antitoxin is well known, and the recurrence of tetanus in the same patient has likewise shown that the disease itself may not confer immunity. Individual immunity may be linked to the occasional harboring of tetanus bacilli in the gastrointestinal tract, and it was the work of Ten Broeck and Bauer<sup>11</sup> that led to the suggestion that immunization could be established by the oral route. The use of toxoid, however, is far simpler and, according to Hall,<sup>12</sup> is completely safe if the toxoid is properly prepared. However, anaphylactic reactions, without fatalities, have been reported from England<sup>13</sup> as occurring twice in 64,000 men immunized for the Royal Air Force. It was found that these 2 persons were sensitive to the Witte's peptone used in preparing the toxoid.

Ramon, the discoverer of toxoid, has recently advised<sup>14</sup> the treatment of acute tetanus as follows: 2 cc. of toxoid subcutaneously and 150,000 units of antitoxin intravenously immediately, and then increasing doses of toxoid every five days, so that the patient receives 4 cc. on the fifth day, 6 cc. on the tenth day and so forth. Such treatment may be effective, but we remain convinced that the constant attention of the nurse and doctor and the employment of the six principles given here are essential to the recovery of the patient severely ill with tetanus.

### SUMMARY

A successfully treated case of tetanus, developing six days after injury, is described in detail.

Six principles of treatment that seem essential to recovery are discussed.

Recently, we have successfully treated another patient using these same principles. The summary of the case, reported through the courtesy of Dr. P. J. Shannon, of Hingham, Massachusetts, is as follows:

On May 27, 1941, a 14-year-old girl cut the dorsum of her right foot on a sickle that was rusted. She was seen within 10 minutes, and the wound cleansed with hydrogen peroxide and Merthiolate. Eight dermal sutures were used to close the wound. Three days later the wound discharged pus, and hot boric acid soaks were applied. On the 4th day fever developed, so sulfathiazole, 1 gm. every 4 hours, was given for the next 4 days. Hydrogen

peroxide dressings to the wound were continued; she seemed improved and was active.

On June 6, 9 days after the injury, she first developed trismus, and by evening she had back pains, headache and malaise; she was given 1500 units of tetanus antitoxin intravenously. The symptoms and signs of tetanus progressed through June 7, and on June 8 she was gravely ill and admitted to the Cohasset Hospital. In the next 24 hours she received 140,000 units of antitoxin intravenously and was given repeated doses of  $\frac{1}{2}$  gr. of morphine. At two periods in the late afternoon she became cyanotic and choked with mucus during the seizures. By evening of June 9, when first seen by one of us (E. M. C.), she was critically ill with severe tetanus and was having generalized spasms or seizures about every 3 to 5 minutes. Local tetanus also caused contractures of the right foot and leg. A culture of the wound was taken immediately and eventually yielded *Cl. tetani*.

Twenty thousand units of antitoxin was injected into three separate areas about the wound before it was debrided and left open. Sulfapyridine was dusted into the wound. Lumbar puncture was done, and dramatic relief of symptoms came after drainage of a clear fluid estimated to be under an initial pressure of 500 mm. Sedation was changed to sodium luminal, about 2 gr. subcutaneously every 3 hours. The nursing care was under the supervision of one of the nurses who had cared for the first patient.

In the subsequent 9 days in the hospital, this girl improved gradually. The lumbar puncture was repeated on June 11, with obvious relief of symptoms. The temperature fell slowly to normal from a level of 102 to 103°F., and the pulse declined gradually from a level of 120. By June 14, swallowing was less difficult and she had regained control of the sphincters. Tetanus toxoid was given as follows: June 12, 1 cc.; June 13, 2 cc.; June 14, 3 cc. Sedation was gradually reduced from a daily total of 16 to 6 gr. On July 18, for economic reasons, she was returned to her home for convalescent care.

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## MEDICAL PROGRESS

### GENERAL ANESTHESIA\*

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**A**LTHOUGH inhalation anesthesia is usually considered synonymous with general anesthesia, other routes of administration of anesthetic drugs must be considered in a discussion of this subject.

#### RECTAL ANESTHESIA

Certain drugs are administered by the rectal route to produce general anesthesia. The most commonly used of these are tribromethanol (Avertin), paraldehyde and the barbiturate, Evipal. Of these, Avertin is probably the best known. These drugs are neither satisfactory nor safe when used alone, but are valuable as adjuncts to other anesthetic agents. They are useful as supplements to nitrous oxide and oxygen when a noninflammable inhalation anesthetic is desired. The administration of one of these drugs in the patient's room is often of great value in allaying the fears of nervous patients. Their principal disadvantages are that proper dosages cannot always be determined, owing to varying rates of absorption from the intestine, and that their administration is often followed by a prolonged period of depression. Because of the prolonged action of these drugs, respiratory obstruction is prone to occur during the postoperative recovery period.

#### INTRAVENOUS ANESTHESIA

The intravenous method of administration of anesthetic drugs has increased in popularity with the introduction of the shorter acting barbiturates. The most commonly used of these are Evipal Soluble and Pentothal Sodium. Their principal advantages are ease of administration and an accuracy of dosage comparable with that of the inhalation anesthetics. Furthermore, induction is usually rapid and pleasant, and recovery as a rule is free from such postoperative discomforts as nausea and vomiting. In common with the rectal anesthetic drugs, they are free from fire hazard.

On the other hand, the intravenous barbiturates have certain disadvantages of which the anesthetist should be cognizant before employing them as anesthetic agents. The margin of safety (the range between the anesthetic dose and the lethal dose) is relatively narrow. Reaction to comparable doses

varies widely, even among patients of the same age and of apparently equal vigor. Since these drugs are largely broken down in the liver and eliminated through the kidneys, they should not be used in patients with impaired liver function or uremia. Because of the means by which the barbiturates are eliminated, there tends to be an accumulation of the drug in the body during prolonged anesthesia. After the anesthesia has been carried on for some time, the addition of very small amounts of these drugs may push the level of anesthesia to a dangerous depth. Under intravenous barbiturate anesthesia, hiccups occur fairly frequently. This is a troublesome complication, the treatment of which is often quite unsatisfactory. The natural tendency when they occur is to increase the depth of anesthesia, this is usually ineffectual and may be hazardous. When anesthesia is light, laryngospasm is prone to occur if the larynx is irritated by operative manipulation or by secretions. For this reason, these drugs are usually not the anesthetics of choice for laryngoscopy and bronchoscopy. In patients with impaired kidney function, recovery may be somewhat prolonged. Finally, many patients, especially those in the elderly group, may be mildly disoriented for a period as long as twenty four hours after waking.

The intravenous injection of barbiturates must be done with care. If a 5 per cent solution of Pentothal Sodium is inadvertently injected into the subcutaneous tissues, marked irritation is likely to occur, and a solution as concentrated as 10 per cent may produce a severe slough. Furthermore, as pointed out by Lundy and Adams,<sup>1</sup> delayed phlebitis may follow the intravenous injection of a 5 per cent solution of Pentothal. For this reason, it is advisable to use a 2.5 per cent solution of this drug intravenously.

A simple and inexpensive apparatus has been described by Nicholson and Sise<sup>2</sup> for the administration of intravenous anesthetic agents. It consists of a small caliber, thick walled rubber tube about 75 cm. in length, with a glass observation tube on one end—to which the needle is fitted—and a stopcock with an adapter for a syringe on the other.

Intravenous barbiturate anesthesia is valuable for short operations when little muscular relaxation is required. It is particularly useful when

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high-frequency electrosurgical apparatus is to be used or when the operative procedure is to be carried out in the x-ray room.

These drugs have recently been used as complements to spinal anesthesia. They should be used only for the comfort of the patient and never to augment a spinal anesthetic that is inadequate or has terminated; an inhalation anesthetic is preferable for this purpose.

#### INHALATION ANESTHESIA

Despite the increase in the use of other routes for the administration of anesthetic drugs, the inhalation method is probably still the most widely employed and the safest in general use, and is certainly the most flexible.

Most drugs used by this method are eliminated largely through the lungs, the liver and kidneys playing a minor part in their removal from the body. Increasing concentrations of the drugs in the blood bring about fairly well-marked changes in the character and rate of respiration, making guideposts by which the anesthetist may judge the depth of anesthesia. The flexibility of this method is such that an anesthetic course may range in depth from mere insensibility to complete flaccidity of most of the skeletal muscles, and in length from a fraction of a minute to many hours. Apparatus for the inhalation method may range from a handful of gauze and a container of anesthetic drug to the most complicated precision gas machines.

Today, although ether is still one of the most satisfactory and widely used general anesthetic drugs, there are many other well-established agents such as cyclopropane, ethylene, nitrous oxide and divinyl ether, which may be administered by the inhalation route, either alone or in combination with ether.

Divinyl ether has a rather limited use. It is a short-acting agent, and when given by the open-drop method is useful when abscesses are to be opened or packs removed or when other brief procedures are to be carried out. Prolonged divinyl ether anesthesia with inadequate oxygen may produce liver damage.

A new anesthetic agent, cyclopropyl-methyl-ether, has been introduced,<sup>3</sup> but its use is still in the experimental stage. Its sponsors state that it is more potent than ether and may possess many of the advantages of cyclopropane.

Cyclopropane, because of its many advantages, has attained great popularity in the few years it has been in use. In many ways, it can still be considered the closest approach to an ideal anesthetic agent that has yet been found. Its extreme potency allows for rapid induction and a very high

concentration of oxygen in the anesthetic mixture. The high concentration of oxygen reduces respiratory activity during anesthesia, but oxygenation has been shown to be adequate.<sup>4</sup> Its effects on the chemical constituents of the body are slight, and it is rapidly eliminated when the anesthesia is terminated.

Cyclopropane, however, has certain properties that prevent it from being an ideal anesthetic agent. Like many other hydrocarbons, it is inflammable. Unmixed with other anesthetic agents, it rarely produces the degree of relaxation required for abdominal surgery unless concentrations are used that are generally accepted as being outside the bounds of safety. Methods have been described and are in use in which concentrations as high as 75 per cent cyclopropane in oxygen<sup>5</sup> are delivered to the patient, and the subsequent apnea handled by artificial respiration or passive breathing. With this technic, the concentration of anesthetic drug is such that the respiratory center is itself anesthetized, and adequate oxygenation is maintained by the pumping of the anesthetic mixture into the lungs by the anesthetist. Relaxation is reported to be as complete as that obtained with spinal anesthesia, and although cardiac irregularities may be observed during induction, they are not found when the required depth of anesthesia is reached. This method is not in general use and seems to be more than a little hazardous except in the hands of those who are highly experienced with it.

Early in the use of cyclopropane, it was found that under fairly deep anesthesia cardiac irregularities developed in a certain number of patients. These are likely to occur with thyrotoxic patients and with those who have impairment of the mechanism of cardiac conduction. It was also found experimentally and, unfortunately, in the operating room that the injection of adrenalin into an animal or patient under cyclopropane produces cardiac irregularities and, in some cases, cardiac arrest probably because of ventricular fibrillation.<sup>6</sup> Laboratory studies on dogs have shown that the irritability of the automatic tissue of the heart is increased by cyclopropane and that morphine tends to increase this irritability further; the barbiturates decrease this tendency to cardiac irregularities to a point where, with deepening anesthesia, respiratory depression precedes their onset.<sup>7</sup> Similar laboratory studies have shown that procaine in small amounts, administered by the intravenous or intracardiac route, arrests the ventricular fibrillation that has been induced by superimposing adrenalin on cyclopropane, and restores normal rhythm.<sup>8</sup> Since procaine is extremely toxic intravenously, it is impractical for clinical use to

prevent cardiac irregularities. Although morphine seems to increase the tendency to cardiac irregularities, and occasionally to subsequent ventricular fibrillation in the dog, it is an extremely useful preoperative drug. Clinically, the barbiturates are not so satisfactory for preoperative medication when used alone as when combined with morphine. Preoperative medication appears to lengthen the margin of safety of cyclopropane by reducing the amount required to produce anesthesia without a comparable reduction in the amount necessary for respiratory arrest.

The majority of cardiac irregularities due to cyclopropane can be eliminated by lessening its concentration in the anesthetic mixture. However, it may be necessary to add another drug to maintain adequate depth. If care is taken that the cyclopropane concentration does not exceed 10 per cent, perceptible cardiac irregularities can usually be eliminated. If this concentration is inadequate to maintain anesthesia, ethylene or ether may be added as a supplement. When ethylene is used as the supplementary agent, the concentration of oxygen must be kept above 20 per cent, or else one of the advantages of cyclopropane, namely, a high concentration of oxygen, is eliminated. A combination of 60 per cent ethylene, 30 per cent oxygen and 10 per cent cyclopropane will give a mixture that is, in most cases, adequate for anesthesia and allows sufficient oxygen. Recovery when cyclopropane and ethylene mixtures are employed, seems to be as rapid as when either of these drugs is used alone.

Cyclopropane may be used instead of ether to supplement ethylene and oxygen or nitrous oxide and oxygen anesthesia. This allows for the administration of adequate oxygen at all times, in addition to the rapid induction and recovery characteristic of gas anesthesia. Although a mixture of ethylene and oxygen permits a somewhat higher concentration of oxygen (15 per cent or less) than that of nitrous oxide and oxygen (10 per cent or less), this is still too narrow a margin to ensure adequate oxygenation. This margin may be further narrowed if the patient has an increased metabolic rate. It must be borne in mind that the absence of cyanosis cannot always be taken to indicate adequate oxygenation.

Although a mixture of nitrous oxide and oxygen is usually inadequate to produce satisfactory anesthesia without suboxygenation, it has the advantage of being noninflammable. Combined with some nonvolatile anesthetic agent, such as intravenous Pentothal or rectal Avertin, it may be used with safety when x-ray or high frequency electrical apparatus is employed. This combination

also permits the use of the cautery about the head and neck.

The explosion and fire hazards present with most inhalation anesthetics are of sufficient importance to require special consideration. Precautions against these hazards should be most careful and painstaking. Ether, cyclopropane and ethylene, when mixed with oxygen, are potential bombs and should be handled with the same degree of respect.

Obviously, no open flames should be allowed in the operating room. If spark proof light switches and wall plugs are not available, all electrical connections should be made and turned on before the anesthesia tanks are opened, and should remain on until the anesthesia is completed and the machine flushed out with air. This flushing of the apparatus can be done by the anesthetist, blowing through the breathing tubes. Electrical equipment in the operating and anesthesia rooms should be carefully and frequently inspected by a qualified electrician. Electric motors and pumps should be placed outside the room when tanks of anesthetic gas are open. If high frequency electrical apparatus is to be used, ethylene, cyclopropane or oxygen and ether should not be administered.

Ether vapor mixed with air probably does not present so great an explosion hazard as ether vapor mixed with oxygen, ethylene and oxygen or cyclopropane and oxygen. Experiments done by Dr. J. W. King,<sup>9</sup> of the Massachusetts Institute of Technology, have shown that no mixture of ether and air will explode with the violence that some mixtures of ether and oxygen do or with the violence that all explosive mixtures of cyclopropane and oxygen do. However, when ether in air is being used in the presence of high frequency electro-surgical apparatus, special care should be taken to deliver the exhaled gases at a point several feet from the site of operation and from the electrical apparatus.

Despite the above precautions, the greatest source of ignition in the operating room, namely static electricity, still has to be dealt with. Obviously, the ideal method for dealing with this hazard would be for every piece of apparatus and all persons in the operating room to be electrically connected. This is not feasible at the present time. If the patient, anesthetist and apparatus (gas machine and operating table) nearest to the explosive anesthetic mixture are electrically connected, a great factor of safety is introduced.<sup>10, 11</sup> The Horton intercoupler\* is an apparatus de-

\*Manufactured by Technipment Company, Brockline, Massachusetts.

signed to connect electrically these four objects in the danger zone.

Inflammable gases should be given in a closed system with carbon dioxide absorption whenever possible, and the room should be adequately ventilated so that leakage of potentially explosive gases may be quickly dispersed. Some work has been done on the quenching value of inert gases such as helium<sup>12</sup> and nitrogen<sup>13</sup> on explosive gaseous mixtures. This may offer an additional safeguard; however, it is still in the experimental stage.

During the administration of a general anesthetic, attention to the maintenance of an adequate airway is as essential as the selection of the anesthetic agent. Nasopharyngeal and oropharyngeal tubes of various kinds relieve respiratory obstruction from the lips and tongue. Complete control of the patient's airway can be ensured only through the use of an endotracheal catheter. By this means, obstruction at the larynx is eliminated, and pressure on the trachea, especially in surgery about the neck, does not result in obstruction to respiration. By means of an endotracheal tube, obstruction from mucus, vomitus and blood may be avoided, since they may be removed by suction. The topical application of 10 per cent cocaine by means of an atomizer allows introduc-

tion of an endotracheal tube with the patient in a fairly light stage of anesthesia and eliminates considerable spasm and coughing when the tube comes in contact with the tracheal mucosa. In patients with marked tracheal obstruction, intubation may be done with topical anesthesia alone, and general anesthesia can be induced after the tube is in place.

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CASE RECORDS OF THE  
MASSACHUSETTS GENERAL HOSPITALANTE MORTEM AND POST MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

## CASE 27431

## PRESENTATION OF CASE

A sixty-two-year old sheet metal worker was admitted to the hospital because of intermittent pain in the abdomen of one week's duration.

For the preceding six to eight years, the patient had been troubled with flatulent indigestion, mild constipation and aversion to fatty foods. On several occasions, he had experienced colic. Nine months before entry, he developed severe knifelike abdominal pain, accompanied by jaundice, and had been seen in another hospital, where cholecystectomy and exploration of the common bile duct were performed. The gall bladder was enlarged and thickened, and the common duct was found dilated, with a number of medium sized faceted stones in its distal end. The liver was described as "mottled." The convalescence was not remarkable, drainage being discontinued on the eighteenth day. The operation seemed to relieve the symptoms except for the intolerance to fatty foods.

Ten days before entry, closely following a meal of stewed chicken, a moderately severe aching pain spread across most of his abdomen. This pain was different from any that the patient had felt in previous attacks in that it seemed more constant and severer, and occurred lower in the abdomen. It continued with only slight remissions until entry. Three or four days before admission, there was gradual onset of jaundice. Increasing amounts of gas were passed by mouth and by rectum. The night before he came to the hospital, the patient vomited slate-colored fluid a dozen times, with some relief.

The past history was not significant. His first wife and his son by her had both died of tuberculosis.

On examination, the patient appeared acutely ill and definitely jaundiced. A right upper abdominal scar was present. The abdomen was tender, especially in the right upper quadrant. The liver was slightly enlarged and tender. External hemorrhoids were present. The only other positive findings were slight enlargement of the heart and

a few basal rales. The blood pressure was 198 systolic, 100 diastolic.

The temperature was 102°F, the pulse 70, and the respirations 30.

Examination of the blood showed a red cell count of 4,000,000 with 60 per cent hemoglobin, and a white cell count of 18,400. The van den Bergh reaction was biphasic, 11.1 mg per 100 cc. The blood sugar was 128 mg per 100 cc (148 mg when repeated). The prothrombin time was 26 seconds. The urine showed a +++ test for albumin, a +++ test for bile pigments and a trace of sugar, on repeated examinations. The stools were not reported.

A flat plate roentgenogram of the gall bladder region was negative. Duodenal drainage was performed, but no bile was found in the sample.

Operative intervention was deferred because of the patient's poor condition. The glycosuria and hyperglycemia were studied but no specific therapeutic measures were taken.

During the first few hospital days, the patient felt improved. The fourth day, however, his temperature rose to 106°F. The liver edge became much more tender, and jaundice deepened. There were no chills or flank tenderness. A roentgenogram of the chest taken in the horizontal position showed the diaphragm to be high, with poor aeration of the lungs. A three day course of sulfadiazine was given, following which the temperature dropped abruptly to 98°F. The drug was discontinued because of a fall in daily urine output to only 150 cc, accompanied by a rise in blood nonprotein nitrogen to 99 mg per 100 cc. The patient became progressively more jaundiced. He was given high carbohydrate therapy and intravenous amino acids. On the fifth hospital day, he vomited several times. Irregularity of the heart was noted. An electrocardiogram demonstrated auricular fibrillation, with a rate varying from 100 to 140 per minute, there were also irregular ectopic ventricular beats. Digitalis was therefore given, resulting in a return to fairly normal rhythm by the ninth hospital day. Four days later, the patient suffered a chill, and his temperature spiked to 104°F. During his last few days, the blood nonprotein nitrogen rose to 270 mg per 100 cc. This was thought to be due to the amino acid therapy he was receiving, since his urinary output had been restored. He became comatose and died on the fourteenth hospital day.

## DIFFERENTIAL DIAGNOSIS

DR. RICHARD H. SWEET: I remember this patient. He came in on the ward a day or so be-

fore I went off service. I do not know what the autopsy showed. He was under the care of Dr. John P. Stewart, who had charge of the cases of common-duct obstruction at that time. My only recollection is that he was exceedingly ill.

We are dealing with an obese, elderly man who was obviously in poor condition at the time of entry. The evidence for that seems to me to be, first of all, the albuminuria, which is also, perhaps, evidence of kidney damage. He may have had diabetes. He had cardiac enlargement with auricular fibrillation and ectopic beats. He had rales in the chest and definite anemia. The second fact that comes to the fore is that he had a known history of gallstones and stones in the common duct removed at operation. The third point I should like to bring out is that he subsequently had a characteristic history of common-duct obstruction, due most likely, I should think, to a stone left in the common duct at the previous operation. I say that because I happen to be a surgeon. The history is very typical. The patient was relieved for a time and felt all right, then had sudden onset of pain, and within a few hours, jaundice and obvious evidence of obstruction. If he had been my patient, I should have thought I had left a stone in the common duct. Secondary to this common-duct obstruction, the record shows evidence of infection of the biliary tract, with chills and fever, the so-called "Charcot syndrome." I should expect that he had cholangitis of an acute nature, with secondary liver damage.

Certain aspects of the case represent complicating factors, chiefly the therapy. One notes that sulfadiazine was given. Then, shortly after that, the sulfadiazine was omitted because of a marked reduction in urinary output and a rise in non-protein nitrogen. This may have been due to the chemotherapy. He may have had kidneys already damaged by arteriosclerosis. It is also known that people with this sort of liver disease do sometimes present evidence of renal damage presumed to be secondary to the liver insufficiency. The argument whether such patients die of liver disease or kidney disease is still a live one, in certain clinics at any rate. The other complicating factor is the amino acid therapy. I am not sure why amino acids were given. The record does not say whether the plasma-protein level was low, or whether he had generalized edema, suggesting perhaps nutritional lowering of the plasma protein; at any rate, he did have amino acid therapy, which I believe had been used very little up to that time on the service, and it probably did account for the marked rise of nonprotein nitrogen, if the

determination was made at the time that the amino acids were circulating in the blood. At that time, the urinary output was not low, and I should assume that the amino acids were not a factor in his death, although that possibility should be kept in mind. I see no evidence for any other conclusion than that he had choledocholithiasis, a stone presumably left in the common duct, in addition to infection, acute cholangitis and, perhaps, liver abscess. He must have had renal damage, whether on the basis of arteriosclerosis or not I do not know. I cannot go so far as to call this a case of hepatorenal syndrome.

#### CLINICAL DIAGNOSES

Cholangitis, acute.  
Multiple liver abscesses.

#### DR. SWEET'S DIAGNOSES

Choledocholithiasis, with obstruction.  
Acute cholangitis.  
Multiple hepatic abscesses?  
Renal damage.

#### ANATOMICAL DIAGNOSES

Cholangitis, with abscess formation and thrombosis of hepatic veins.  
Subhepatic abscess, probably at site of amputated gall bladder and cystic duct.  
Icterus, generalized.  
Pulmonary collapse and congestion, bilateral.  
Pancreatitis, minimal.  
Bile nephrosis.  
Decubitus ulcer, right buttock.  
Obesity.

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: Some of the findings post mortem were quite obvious. The patient did have very extensive sepsis in the biliary tract, with a diffuse intrahepatic cholangitis and multiple liver abscesses. There was also a subhepatic abscess, in the immediate area of the removed gall bladder, a large, well-localized pocket of pus about the size of a distended gall bladder. There were no persisting stones in the duct; they had all been removed. The heart was somewhat hypertrophied, suggesting that he may well have had some hypertension and perhaps some renal insufficiency based on that, although the kidneys showed no striking degree of nephrosclerosis. At the time of autopsy, we were impressed with a little discoloration at the junction of the pyramids and cortex, which we thought might possibly be crystals of sulfapyridine, and in view of his terminal anuria we naturally attempted to establish that

point. We could not. There were no crystals, and I think the discoloration was due to bile-stained casts, rather concentrated at that point in the tubules. The kidneys were grossly swollen, and the cells of the convoluted tubules were likewise swollen and contained moderate amounts of bile pigment, the picture of what has been called bile nephrosis. That is something that one sees with considerable regularity in deeply jaundiced patients. So far as I can make out, its severity bears no correlation to the presence or absence of the so called "hepatorenal syndrome." I should be tempted to think that this man died from the combination of sepsis and hepatic insufficiency, and rather discount any renal factor, although on anatomic grounds it is impossible to do so with certainty. I should think that with such extensive liver disease as this, one ought to use caution in amino acid therapy. We know that amino acids are deaminized solely in the liver, and in the face of a nonfunctioning liver I do not see how the organism can dispose of them.

DR SWEET: It seems to me that that is the important thing about this case. As I read it over, I wondered what amino acids and the sulfadiazine had to do with his death. But he was an extremely sick man and probably would have died anyway of his underlying disease.

DR MALLORY: So far as the anatomical evidence goes, we can rule out the sulfadiazine as the cause of renal insufficiency.

## CASE 27432

### PRESENTATION OF CASE

A sixty two year-old housewife entered the hospital because of repeated episodes of pain in the chest.

Nothing was known about the first attack, except that the pain had been mild and had involved the left chest approximately six months before entry. The second episode, two months before admission, consisted in a moderately severe pain in the left chest accompanied by an ache in the left elbow. There was no radiation of pain to the shoulder, and there was no respiratory difficulty. The patient's physician prescribed a course of theobromine, potassium iodide and phenobarbital. At the time of this attack, the blood pressure was 164 systolic, 104 diastolic, the pulse 84, and the temperature 98.1°F. The following day the blood pressure was 140 systolic, 80 diastolic, the pulse 72, and the temperature 98.3°F. On the third day, the blood pressure was 130 systolic, 90 diastolic, and the pulse and temperature remained as before.

The patient was kept in bed for six weeks and then allowed up. The next day, she experienced minor chest pain. About ten days later,—ten days before entry,—pain again appeared, this time in the right chest, radiating to the shoulder and also across the abdomen. Three days before admission, there was an insidious onset of slight painless coughing. In the evening, a spell of severe coughing lasted six or seven minutes. During the night, the patient perspired freely and her heart seemed to "beat twice as fast as normal." The following day, she complained of a sensation "like a collection of gas" below the right breast, more disturbing when she coughed. Her local physician gave morphine and began a course of sulfathiazole.

The patient had had varicose veins for years and remarked that she had had a "sore spot" behind her left knee about ten days before she came to the hospital.

Physical examination showed an elderly and slightly obese woman, who was not acutely ill. She was pale, with cyanotic lips. Her respirations were grunting and cut short by pain, and there was definite splinting of the right chest. The breath sounds were diminished at the right base, with many crackling rales. The heart sounds were poor, although they seemed accentuated over the mitral area. The blood pressure was 120 systolic, 90 diastolic.

The pulse was 104, and the respirations were 28.

A roentgenogram of the chest showed the diaphragm to be high on both sides. In the left lung field, a band of density obscured the lateral shift of the diaphragm. On the right, there were numerous linear bands and some haziness just lateral to the hilus. The upper lung fields were clear, and the heart shadow was not displaced.

During physical examination, the patient suddenly turned ashen. Her lips became more cyanotic, and beads of perspiration stood out on her face. There was partial loss of consciousness. The respirations became more rapid. Morphine, atropine and Coramine were given, and the patient was placed in an oxygen tent. In the course of fifteen minutes, the respirations became slower and more shallow; death followed, an hour and twenty minutes after admission.

### DIFFERENTIAL DIAGNOSIS

DR RENO PORTER: Here is the case of a woman who, except for varicose veins, was in good health and feeling well until six months before admission. She subsequently experienced four attacks of chest pain. There were no other significant signs or symptoms, such as cough, respiratory dif-

ficuity and changes in pulse and temperature, and no change in blood pressure. The fact that the location of the pain varied from one attack to another tends to rule out many localized processes originating in the lungs themselves. The last attack was ten days prior to admission, when the patient also noted a sore spot behind her left knee. This is a very important point and gives some indication about the origin of most of her difficulties, namely, a phlebitis. However, one could suspect such an origin without this evidence, because pulmonary emboli usually occur repeatedly before the offending phlebitis becomes obvious. For three days before admission, the patient had symptoms indicative of pleurisy, with cough, splinting of the right side of the chest, pain on respiration and x-ray evidence of multiple lung lesions. Then she died abruptly, soon after she was admitted.

It is quite evident from the data presented that she had repeated pulmonary emboli. The terminal event was probably massive pulmonary embolism. I think one can conclude this from the repeated attacks of chest pain, a story quite characteristic of pulmonary infarction, and also from the fact that x-ray examination showed evidence of multiple lesions. One would, perhaps, like a little more evidence, such as symptoms and signs of respiratory difficulty, as well as temperature and pulse changes. They were not present, but their absence does not rule out the possibility, because embolism can occur without objective evidence.

The question in my mind is whether this entire story can be explained on the basis of pulmonary emboli. It has been generally assumed, and I for a time had the impression, that pulmonary emboli are nearly always secondary to something else, commonly following a surgical procedure or occurring as a complication of heart disease. Hampton and Castleman<sup>1</sup> have shown that this is not necessarily so by their study of 307 cases of pulmonary infarction. They found that in 30 per cent the patients were nonsurgical and noncardiac. This patient, we know, had not been operated on, so that there was no predisposing factor. The heart on physical examination was normal in size, with no significant murmurs. She did have hypertension, however. One cannot definitely rule out the possibility that one of these attacks of pain was coronary thrombosis. Her doctor apparently thought that she had had a coronary thrombosis, since she was kept in bed for six weeks. The onset of chest pain, however, is the only indication. There were no other striking signs or symptoms, nor is there an electrocardiogram to help us. There was apparently no significant

drop in blood pressure. The blood pressure fell somewhat in bed, but this could be explained by bed rest alone. There is very little evidence on which to make the diagnosis of coronary thrombosis.

Other conditions that might have occurred, such as infection, which her doctor suspected because he gave her sulfathiazole, need not be considered here. She did at one time complain that her heart beat more rapidly than normal. One must think of the possibility of an arrhythmia producing emboli that might go to the lungs. This tachycardia occurred during only one attack of pain, with no subsequent reference to irregularity. I think that this can be dismissed as a simple reaction to any insult to the lung.

I shall make a single diagnosis of multiple emboli. They arose probably from a thrombophlebitis of the popliteal vein on the left and possibly from the varicosities she had on the right. The emboli were multiple, and there should be infarctions of the lung, both old and recent. She may have had some pleural effusion on the right, associated with infarction, and I think she died of massive pulmonary embolism.

**DR. PAUL D. WHITE:** It is rare to find coronary episodes in the form of coronary thrombosis recurring repeatedly over a period of a few months. I therefore think that although pain was the characteristic symptom in the beginning in this case, the frequency of the attacks is very much against myocardial infarction as the explanation of the whole story. As Dr. Porter says, coronary thrombosis may have begun the sequence of events, but the later "heart attacks" were in all probability due to pulmonary emboli.

The hypertension we know very little about; there is simply a record of a blood pressure of 164 systolic, 104 diastolic, at the time of the attack. This may have been a rise, the result of pain or discomfort, but on the other hand, the pressure might have dropped to this level; so that myocardial infarction might have been present despite the relatively negative examination. We do not have a definite statement about the heart size, simply the signs; we should expect, however, that the x-ray report would have shown cardiac enlargement. Tachycardia is common in pulmonary embolism. It may be the only symptom of an attack of pulmonary embolism, and paroxysmal tachycardia may be wrongly diagnosed to explain such episodes as occurred in this case, which I think Dr. Porter has correctly interpreted.

#### CLINICAL DIAGNOSES

Recurrent coronary thrombosis.  
Pulmonary embolism.

## DR. PORTER'S DIAGNOSES

Thrombophlebitis, left popliteal vein  
Multiple pulmonary emboli.  
Pulmonary infarcts, old and recent  
Massive pulmonary embolism.

## ANATOMICAL DIAGNOSES

Coronary thrombosis.  
Myocardial infarction.  
Thrombosis of popliteal vein, left  
Multiple pulmonary infarcts.  
Acute massive pulmonary embolism

## PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN This patient had, as Dr. Porter predicted, numerous infarcts in the lung. They were present in every lobe of the right lung, more numerous in the lower lobe, and were of varying sizes and ages. There was no pleural fluid, but the pleura was fibrinous over the lower lobe. The main branches of the pulmonary artery were filled with emboli, and one large embolus was present in the right ventricle, extending through the pulmonary valve. The source of the emboli was in the left leg—the popliteal vein and many of its branches and tributaries were completely filled with thrombi. The heart weighed 375 gm. and showed slight hypertrophy. The coronary arteries showed severe sclerosis, with occlusion and narrowing. The left descending branch was almost completely occluded by a grayish thrombus, which might have been two or three months old. The anterior wall of the left ventricle was infarcted, and according to the criteria that were reported a few years ago by Mallory, White and Salcedo Salgar<sup>2</sup> on the various ages of myocardial infarcts, was about two months old. This would correspond with the second episode. I therefore suppose that the patient

started off, as Dr. White suggested, with a coronary thrombosis, was kept in bed for six weeks, allowing the peripheral thrombi to form while she was in bed, and when she got up developed a series of emboli and infarcts. Is it a general procedure to exercise the legs of patients with coronary disease?

DR. WHITE: Rest in bed for two months is much too long for the average person with acute coronary thrombosis and myocardial infarction, particularly because of the danger to the general health, especially from thrombophlebitis. There are, to be sure, some patients with congestive failure or other complications who may have to stay in bed longer, but as a rule, for patients with average-sized infarcts three or four weeks in bed are enough. Some have thought me unwise in advising such a short stay, but experience has confirmed its adequacy, in fact its preference. The chair position, incidentally, is better than the bed position so far as the heart is concerned. Instituting activity as soon as possible aids the peripheral circulation, as well as the morale and general health. I suppose we all tend to neglect to maintain adequate peripheral circulation in bed patients, which we can do by massage and even by active leg exercise. After the first two weeks, as soon as danger from the acute heart attack is largely over, the leg muscles need massage or exercise.

DR. HOWARD B. SPRAGUE: I have done that routinely for years. As soon as the fever is over, I start leg massage and encourage the patient to move the feet and wiggle the toes.

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## ENCEPHALITIS AND THE HORSE

ONCE again, the importance of animal reservoirs of diseases affecting human beings comes to the fore. Recent work<sup>1-4</sup> from the West indicates that the virus of the St. Louis type of encephalitis is present in certain wild and domestic birds and mammals.

Especially in the group of encephalitides due to specific viruses has the role of animals become increasingly evident. About six months ago, Webster<sup>5</sup> pointed out that no less than nine distinct viruses—those of rabies, poliomyelitis, lymphocytic choriomeningitis, Japanese B encephalitis, louping ill, Australian X disease, virus B, equine encephalomyelitis and St. Louis encephalitis—are known to produce primary encephalitis in man.

At that time, there was good evidence of mammalian or avian host reservoirs for six of these agents. The virus of rabies was demonstrated in animals in 1881. During the last decade, the virus of lymphocytic choriomeningitis was found in the mouse, that of louping ill in sheep, that of virus B in the monkey, and that of equine encephalomyelitis in horses and birds. Furthermore, the serums of sheep and horses have been found to contain neutralizing antibodies for the virus of Japanese B encephalitis. All these diseases were thus linked with animals. Only three viruses—those of poliomyelitis, Australian X disease and St. Louis encephalitis—gave no evidence of potential animal reservoirs.

Now, however, the virus of St. Louis encephalitis, as well as that of the Western type of equine encephalomyelitis, has been incriminated in both horses and human beings in the Yakima Valley of Washington by the work of Hammon,<sup>1</sup> and in Weld County, Colorado, by that of Philip, Cox, Fountain and Kilpatrick,<sup>2,3</sup> of the United States Public Health Service. The presence of neutralizing antibodies in the serums of patients and horses indicated infection in some cases with one of these viruses, and in others with both. Similar evidence for mixed infection with the same viruses in human beings in California had previously been presented by Howitt.<sup>6</sup>

In the Yakima valley, the epidemics occurred during the two summers of 1939 and 1940. As might be expected in an outbreak due to two different agents, certain epidemiologic and clinical features were suggestive of each of the two types of encephalitis, although the general picture was more comparable to that of the St. Louis epidemic of 1933 than to any of the known equine-encephalomyelitis epidemics. Most of the patients lived near irrigation ditches or other potential sites of mosquito breeding. The possibility of insect vectors was not further investigated, but probable reservoirs for one or both viruses were suggested by the finding of neutralizing antibodies in the blood serums of a certain number of wild and domestic birds and mammals.

The reports from Weld County present similar

evidence of human infection with either one or both of these viruses. They further show that the serums of certain horses, not only from Colorado, but also from Montana and Washington, contained neutralizing antibodies for one or both viruses. The disease was reproduced experimentally in susceptible horses by the intracerebral inoculation of a proved strain of St. Louis virus. The resulting infection was indistinguishable clinically from that caused by the Western strain of equine-encephalomyelitis virus. It is thus evident that the differential diagnosis on clinical grounds is difficult, if not impossible.

Of even more interest, however, was the observation that during the course of this disease the infective agent was found in the nasal secretions but could not be detected in the blood. From the epidemiologic standpoint, therefore, it seems unlikely that transmission from the horse could be accomplished by blood sucking insects. Moreover, since the virus is present in nasal secretions, transmission may be possible by direct contact, by vectors such as the common housefly or horsefly, by fomites, by water and so forth. These findings obviously provide a fertile field for further research.

More recently Hammon and his co-workers<sup>7</sup> have isolated the viruses of western equine and St. Louis encephalitis from mosquitoes (*Culex tarsalis*) collected from areas in which human encephalitis cases occurred. This evidence suggests the vector. Several species of wild and domestic birds and mammals may then be the important host reservoirs,<sup>4</sup> whereas the horse remains only an accidental victim.

Effective therapy for these types of encephalitis is lacking. Specific therapeutic antiserums are of no avail at the present time because a sufficiently early etiologic diagnosis cannot be made. Prophylaxis with virus preparations, particularly for animals, offers some hope, but has not yet been investigated thoroughly enough. Particularly in view of the present defense program and the concentration of troops in camps, continued study of host reservoirs and methods of transmission is urgently needed to control these summer epidemics.

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## MAN ON HIS NATURE\*

SIR CHARLES SHERRINGTON, the dean of British physiologists, and long the chief exponent of structural neurology, whose life has been devoted to the elucidation of the reflex actions of the nervous system in its component parts and the integration of this action in the brain, was a particularly happy choice as Gifford Lecturer at Edinburgh in 1937-1938. Who better than Sherrington could, to quote his own words, use natural science to provide a frame of reference for Natural Theology? With the outlook of a poet, he provides science's generalizations about nature, using as a comparison the ideas on the same subject of Jean Fernel, a French physician of the mid-sixteenth century, who wrote *On Hidden Causes* (Paris, 1542), the first modern textbook of physiology.

Sherrington first points out the great changes in science that have occurred in the four hundred years since Fernel's time. Dealing with hard facts, the mechanical behavior of electrons, for example, we hardly talk the same language or think and research with the same tools. Science still, however, deals with facts, and facts only—smaller and smaller, to be sure, but still concrete. We can look at nature only with them in mind, but since man is part of nature, we can also look at man, although with slight understanding. We see brain, cells and processes, and even diagrammatically satisfy ourselves regarding reflex action. But how can we envisage "mind"? Energy does not seem to answer the question. Sher-

\*Sherrington C S. *Man on His Nature*. The Gifford Lectures, Ed. N. Lush, 1933-1938. 413 pp. New York: The Macmillan Company, 1941.

Sherrington concludes that "mind" for anything "... perception can compass goes therefore in our spatial world more ghostly than a ghost. Invisible, intangible, it is a thing not ever of outline; it is not a 'thing.' It remains without sensual confirmation, and remains without it for ever. Stripped to nakedness there remains to it but itself. What then does that amount to? All that counts in life. Desire, zest, truth, love, knowledge, 'values,' and, seeking metaphor to eke out expression, hell's depth and heaven's utmost height." To this concept of "mind," Sherrington adds "the perceived world. . . . Together they make up the sum total for us: they are all we have."

This, and much more, will be found in this thought-provoking book, a scholarly treatise such as is rarely given to the world. Not by any means easy reading, it will provide rich nourishment, if slowly digested. In a busy, war-torn world, too few will have time for such an intellectual treat; but *Man on His Nature* will last, and no doubt will be read four hundred years from now, just as Sherrington reads Fernel's *On Hidden Causes*.

## MEDICAL EPONYM

### KORSAKOW'S SYNDROME

Sergei S. Korsakow (1853-1900), privatdocent of the Imperial University in Moscow, described the syndrome that bears his name in an article entitled "Ueber eine besondere Form psychischer Störung, combinirt mit multipler Neuritis (A Peculiar Form of Psychic Disturbance Associated with Multiple Neuritis)" in the *Archiv für Psychiatrie und Nervenkrankheiten* (21: 669-704, 1889). He refers to his first report on the subject, which appeared in a Russian journal, *Westnik Psychiatrii*, during 1887 under the title, "Disturbances in the Psychic Sphere Occurring in Alcoholic Paralysis, and Their Relation to the Psychic Disturbances in Multiple Neuritis of Nonalcoholic Origin." A portion of the translation follows:

This psychic disturbance is shown sometimes in the form of a well-marked irritable weakness of the psyche, sometimes in the form of confusion, with quite characteristic disorientation in regard to place, time and situation, again as an almost pure variety of acute amnesia, with the most extreme sort of disturbance in the memory for recent events, while remote occurrences are well remembered. This unique psychic change is almost constantly present to a greater or less degree in the multiple neuritis of alcoholic patients; it

is not, however, an exclusive characteristic of alcoholic neuritis, but also occurs in neuritides due to a variety of other causes.

R. V.

## MASSACHUSETTS MEDICAL SOCIETY SECTION OF OBSTETRICS AND GYNECOLOGY\*

### FATAL SHOCK, FOLLOWING PLACENTA PREVIA AND MASSIVE HEMORRHAGE

A thirty-six-year-old para X entered the hospital, when approximately seven months pregnant because of a sudden massive hemorrhage.

The patient had eight living children, and she had been one miscarriage. The last pregnancy was terminated by a cesarean section, and a living child weighing 9 pounds, 9 ounces, was delivered. The section was indicated because of an amputated cervix, and the repair of a third-degree tear of the perineum.

The patient had bled a little several times during the previous two months. Two weeks before admission, she had bled sufficiently so that a diagnosis of placenta previa was considered, although no vaginal examination was made. An x-ray film taken for the purpose of diagnosis did not show a placenta previa. On the day of admission, the patient had a very sudden massive hemorrhage at home and was sent to a hospital, where a vaginal pack was inserted. From this hospital, she was transferred to another institution, where the first pack was removed and a second introduced; a central placenta previa was found. Because the bleeding was excessive, cesarean section was performed immediately. A living child was delivered but died shortly after birth. The patient died four and a half hours after operation. The patient was apparently not transfused; the record states that she died of shock.

*Comment.* From the obstetric point of view, this patient was not ideally handled, and the fatal result should have been averted. Any patient who bleeds in the last trimester is entitled to an intelligent search for the cause of the bleeding. No intelligent diagnosis can be made without a vaginal examination. This patient was seen several times because of this bleeding, but at no time was a vaginal examination made. Had one been made and the cervix investigated, the central placenta previa would have been diagnosed, and the operation might have been done at election, not when the patient was weakened by excessive hemorrhage.

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, Secretary, 330 Dartmouth Street, Boston.



and in moderate shock. X-ray study in the diagnosis of placenta previa is not always reliable; it should never take the place of a thorough and intelligent vaginal investigation.

The previous cesarean section made a second section imperative. No patient is so badly off that transfusion before operation is not of inestimable value, because any patient who succumbs while being transfused certainly would not survive, no matter what was done to her. It is barely possible that immediate transfusion, followed by operation, might have tided her over, but this is only problematical.

The lesson to be learned from this case is that all patients with bleeding in the last three months of pregnancy should be hospitalized, a definite diagnosis of the cause of bleeding made by vaginal examination, even at the expense of invading the cervical canal, and subsequent treatment based on this diagnosis given at the time of election. It is routine in most obstetric institutions that, when a vaginal examination is attempted on bleeding cases of this sort, a bagging kit and a laparotomy kit are both in readiness and an acceptable donor is at hand. It is only by following this technic that such fatalities can be averted.

## DEATHS

**BURNS**—HIRAM H. BURNS, M.D., of Plymouth, died May 10. He was in his eighty-sixth year.

Dr. Burns received his degree from the Harvard Medical School in 1887 and was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow survives him.

**KRANTZ**—MICHAEL KRANTZ, M.D., of Quincy, died September 4. He was in his sixtieth year.

Born in Russia, he received his degree from Middlesex University School of Medicine in 1921. He was a fellow of the Massachusetts Medical Society and of the American Medical Association.

His widow survives him.

**MURPHY**—DANIEL D. MURPHY, M.D., of Amesbury, died August 8. He was in his seventy-eighth year.

Dr. Murphy received his degree from the Dartmouth Medical School in 1891. At the time of his death, he was on the staffs of the Anna Jaques Hospital, Newburyport, and the Amesbury Hospital. He was a former president of the Essex North District Medical Society, and was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow and two sons survive him.

## MISCELLANY

### RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR AUGUST, 1941

DISEASE	AUGUST 1941	AUGUST 1940	FIVE YEAR AVERAGE*
Anterior poliomyelitis	45	9	36
Chicken pox	125	81	105
Diphtheria	6	12	14
Dog bite	1043	1178	1112
Dysentery, bacillary	30	15	14
German measles	31	20	24
Gonorrhea	283	366	457
Measles	282	506	277
Meningitis meningococcal	4	3	5
Meningitis, other forms	4		
Mumps	274	157	137
Paratyphoid fever	8	36	17
Pneumonia, lobar	74	91	110
Scarlet fever	196	77	110
Syphilis	341	297	415
Tuberculosis, pulmonary	281	298	301
Tuberculosis, other forms	26	25	31
Typhoid fever	9	11	11
Undulant fever	13	1	4
Whooping cough	575	505	511

\*Based on figures for preceding five years

### GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Actinomycosis was reported from: Malden, 1; total, 1.

Anterior poliomyelitis was reported from: Beverly, 1; Boston, 4; Brockton, 3; Cambridge, 4; Dudley, 1; Leominster, 1; Fairhaven, 1; Haverhill, 2; Lawrence, 1; Lynn, 2; Malden, 1; Melrose, 1; Methuen, 5; New Bedford, 9; Northbridge, 1; Provincetown, 1; Quincy, 1; Somerville, 1; Taunton, 1; Uxbridge, 1; Wareham, 2; Worcester, 1; total, 45.

Anthrax was reported from: Peabody, 1; total, 1.

Diphtheria was reported from: Fall River, 5; Wrentham, 1; total, 6.

Dysentery, amebic, was reported from: Fitchburg, 1; total, 1.

Dysentery, bacillary, was reported from: Boston, 1; Braintree, 1; Cambridge, 1; Danvers, 7; Ipswich, 1; Melrose, 1; Medford, 1; Stoneham, 1; Watertown, 1; Worcester, 15; total, 30.

Infectious encephalitis was reported from: Cambridge, 1; Fall River, 1; New Bedford, 1; total, 3.

Malaria was reported from: Framingham, 1; total, 1.

Meningitis, meningococcal, was reported from: Cambridge, 1; Stoneham, 1; Wareham, 1; Yarmouth, 1; total, 4.

Meningitis, other forms, was reported from: Arlington, 1; Boston, 1; East Bridgewater, 1; Weymouth, 1; total, 4.

Paratyphoid fever was reported from: Beverly, 1; Cambridge, 1; Fort Banks, 1; Ipswich, 1; Lynn, 1; Medford, 2; Peabody, 1; total, 8.

Pellagra was reported from: Boston, 1; Peabody, 1; total, 2.

Septic sore throat was reported from: Boston, 1; Cambridge, 1; Greenfield, 1; total, 3.

Tetanus was reported from: New Bedford, 1; total, 1.

Trachoma was reported from: Fall River, 1; Nauck, 1; total, 2.

Trichinosis was reported from: Boston, 1; Worcester, 1; total, 2.

Typhoid fever was reported from: Ayer, 1; Boston, 4; Deerfield, 1; Fall River, 1; Marblehead, 1; North Adams, 1; total, 9.

Undulant fever was reported from: Brookfield, 1; Deerfield, 1; Falmouth, 1; Franklin, 1; Haverhill, 1; Hopkinton, 1; Leominster, 1; Medford, 1; North Adams, 1; Orange, 1; Sheffield, 1; Uxbridge, 1; Worcester, 1; total, 13.

For the sixth consecutive year anterior poliomyelitis failed to reach epidemic proportions by the end of August.

Undulant fever was at a high level during the month.

Mumps and meningococcal meningitis both tended toward higher levels, though they have shown the usual seasonal decline.

Chicken pox, bacillary dysentery, scarlet fever and whooping cough were slightly above the five-year average. Diphtheria, lobar pneumonia and typhoid fever were at unusually low levels.

Dog bite, gonorrhea, paratyphoid infection, syphilis and pulmonary tuberculosis were reported below the five-year averages.

Measles and German measles, which showed increased prevalences earlier in the year, made a rapid seasonal decline.

### X-RAYING MILITARY MEN

Experience in World War I showed the value of discovering tuberculosis among military men. When the Selective Service Act went into effect, the Navy was requiring a chest roentgenogram for all enlisted and commissioned men, and the Army for the commissioned personnel only; facilities for routine roentgenography of all men were not at first available. Among the civilian agencies that supplemented the efforts of the Army in this emergency was the Bureau of Tuberculosis of the New York City Department of Health. These abstracts are taken from a record of that organization's experiences (Edwards, H. R., and Ehrlich, D. Examinations for tuberculosis, *J. A. M. A.* 117:40-45, 1941).

An order issued October 28, 1940, by the Adjutant General's Office of the United States Army made it possible for civilian organizations to set up a roentgenographic service for men inducted into the Army. It provided for payment for x-ray films and for the services of civilian roentgenologists (under due control) until such time as the Army could assemble its equipment and assume full responsibility.

The Bureau of Tuberculosis of the New York City Department of Health has been engaged in mass roentgen-ray surveys of the apparently healthy population since 1933. These surveys have been accepted as a basic part of the tuberculosis-control program of New York City, and thus interest, based on experience, in providing a similar service for inductees and members of the State National Guard was keen. Accordingly, the bureau's mass roentgen-ray services, which were made possible through the WPA, were offered to the Surgeons of the Second Corps Area prior to the Adjutant General's order. Financial assistance was received from the tuberculosis associations of Queens and the Bronx.

After January 1, 1941, the Army assumed full financial responsibility for the roentgen-ray service in induction centers. The Department provided personnel for the interpretation of films. Since January 15, this service has also been taken over by the Army, which has assigned medical reserve officers qualified in this special field. The roentgenographing of National Guardsmen has been entirely at the expense of the Department of Health. Under existing regulations, the Army could not pay for this service until after induction, and it was essential that rejections be made before induction.

At the outset, there were four induction stations. Since January 1, 1941, all work has been done in two stations, one in Manhattan and one in Queens.

Those rejected men who were residents of New York

City were given an appointment within the next two or three days to appear at the Health Department's Central Chest Clinic, where a complete study of the case was made. If this examination proved the original findings to be of no significance, the local draft board was so notified.

Rapid roentgenographic service was necessary, since the recruit was supposed to be cleared through all examinations by 2:30 p.m. of the day he reported at the induction station. With from 60 to 300 men per unit to be handled daily, even the rapid roll method used in the routine survey program was inadequate. Consequently, a special type of apparatus was devised. A modification of the roll paper camera was used in connection with a specially constructed portable dark room measuring 8 by 8 feet, with the back of the camera integrated into one side of the dark room. A signal device was installed between the roentgen-ray technician and the dark room. As soon as a film was exposed, the signal was flashed, and the dark room crew cut off the film and placed it in the developing bath. The signal was then reversed, indicating that another film was ready to be exposed. A team of three, consisting of a technician and two dark-room assistants, were able to operate faster than one exposure a minute. The films were processed in large trays and from the fixing bath were passed out to the physician through a light-proof pass. After being read, the films were washed in a portable tank and dried in a special device designed for the purpose.

Acceptance or rejection was based on Army regulations. Men showing any form of reinfection types of tuberculosis were rejected, because lesions of such types may become aggravated under conditions of military service. Primary lesions considered as active or extensive calcifications were likewise cause for rejection. Other forms of significant pulmonary disease, such as bronchiectasis, pneumonitis, atelectasis and extensive pleural changes, were cause for rejection until further study could determine their importance. Men with obviously abnormal cardiac silhouettes were reported to the medical examiners for such further study as might be indicated. Men with nothing more than apical caps, and those with small well-healed primary lesions were not rejected.

The group of men examined up to January 15, 1941, a period in which the Department of Health was actively engaged in the program, included 6609 inductees and 9541 guardsmen, a total of 16,150 who were x-rayed.

Of the inductees, 1.36 per cent were rejected and of the guardsmen, 1.21 per cent. About one third of the guardsmen were below the age of twenty-one, whereas only about 0.5 per cent of the inductees were below that age. An all-Negro regiment (National Guard unit) had the highest mean age in all groups and the highest rate of rejection, which was almost entirely on the basis of pulmonary tuberculosis. If the findings in this unit are subtracted from the totals of all National Guard units, a greater difference will be found between guardsmen and inductees.

Classification by stages of disease of the 70 men whose lesions were considered clinically significant shows that 65.7 per cent were minimal, 32.9 per cent moderately advanced and 1.4 per cent far advanced. Primary lesions indicated by calcific deposits were found in 6 per cent of the white men, 8.7 per cent of the Negroes and 7.1 per cent of the Puerto Ricans.

The group of men examined since January 16 and through March 31, 1941, totaled 35,210 men. During that period, the Department of Health's part has been

to re-examine and classify New York City men rejected at the induction center. In this time, 458 men have been rejected, 379 of whom have thus far been cleared at the Health Department Clinic. In 49, or 12.9 per cent, of those re-examined, the cause for rejection at the induction station was not confirmed, and the man was therefore considered suitable to be accepted in the Army.

A detailed cost analysis of personnel, equipment and materials necessary to complete this study indicated a total of \$23,614.20. Using this as a basis for computation, the unit cost to examine each man by roentgenogram was \$147 (the cost of taking a roentgenogram and its interpretation without any further follow up was \$13.91, 20, or 58.8 per cent of the total). The unit cost of rejecting a man for military service on the basis of the total cost was \$106.02 for inductees and \$122.37 for guardsmen.

Spillman has reported that the cost to the federal government of accepting a person with tuberculosis into the armed service is \$10,000. Thus, in these studies involving 41,819 inductees and 9541 guardsmen, or a total of 41,360 men, 561 persons with chronic pulmonary tuberculosis were rejected, representing an estimated saving to the government of \$5,610,000.—Reprinted from *Tuberculosis Abstracts*, October, 1941.

## NOTES

The following appointments to the teaching and research staff of the Harvard Medical School were recently announced by the University (effective this year): Norbert A. Wilhelm, M.D., St. Louis University School of Medicine, 25 lecturer on public health practice; William V. Knoll, M.D., College of Medical Evangelists, 35 Lucas N. Littauer Fellow in Pathology at the Collis P. Huntington Memorial Hospital, and Edward J. Welch, M.D., Harvard, 36, assistant medical adviser.

Dr. Leon K. Baldauf has been appointed to a full time professorship as head of the Department of Pathology at the School of Medicine at Middlesex University. He was formerly assistant in pathology at the Albany Medical College, resident pathologist at St. Louis City Hospital and professor of pathology and bacteriology at the University of Louisville School of Medicine, for the last three years, Dr. Baldauf has served as pathologist at the Cambridge City Hospital.

## CORRESPONDENCE

### PREMARITAL MEDICAL EXAMINATIONS

To the Editor: In reading the October 7 issue of the *Journal*, I came across Dr. Allen Johnson's remarks concerning premarital examinations on those persons who for several months or years have been traveling in the clouds of that grand passion and for the first time are about to put their feet once more on solid ground. What a rude awakening for the prospective groom to have a gloved finger roughly rammed through a spastic sphincter to massage a prostate in search of evidence of his past indiscretions.

Frankly, I believe there are a lot of us who are pretty much in the dark as to how far such an examination should be carried. Should it rest with a routine sample of blood or should smears also be taken? I think it would be of great help if there were some discussion of this in the *Journal*, and possibly a printed outline covering the essentials of such an examination in both men and women. Possibly some short form of examination sheet could be devised that could be incorporated with the regular history form, this would give uniform charac-

teristics throughout the State instead of a hit-or-miss sort of affair. Furthermore, if a patient could be shown such a blank and told this is the regular form sponsored and approved by the Massachusetts Medical Society and used by every physician in the State, I do not believe there would be much antagonism to taking of general smears. The man or woman would merely think, 'All the others have to go through the same procedure, so why should I complain?' I think this would greatly lessen the embarrassment of both parties, give a truer picture of the possibility of genitoinfectious disease and tide the doctor through the necessary procedures. I believe that such a slip of paper would well prove its worth to all concerned.

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## BOOK REVIEWS

*Shock: Blood studies as a guide to therapy*. By John Scudder, M.D., Med.Sc.D. 4°, cloth, 323 pp with 55 illustrations and 5 plates, 3 in color. Philadelphia: J. B. Lippincott Company, 1940. \$5.50.

This volume reviews the whole subject of shock and advances as the author's special contribution the theory that the increase in the potassium content of the plasma observed in shock (as in most cases of tissue injury) is in fact an evidence of potassium poisoning that plays a part in causing the shock syndrome, and the recommendation of adrenocortical hormone (Eschmann) as an important chemotherapeutic measure—based on the belief that it tends to restore blood volume and relieve hemoconcentration, to raise blood pressure, to combat decrease in alkali reserve by aiding the retention of bases and to promote excretion of potassium and ammonia by the kidney, and that it accomplishes a number of other desirable things. The reader must decide for himself to what degree these beliefs are substantiated. Concerning potassium, it is clear that the diminution of effective blood volume, which is admittedly an underlying cause of the shock syndrome, precedes the hyperkalemia; there appears to be no evidence of an adrenocortical insufficiency in shock, although the use of the extract by the author in connection with other standard measures seems to have had good results.

Section I gives a historical introduction in three pages, Section II, on the theories of shock, is an enumeration of authorities supporting or opposing the responsibility of toxemia, the loss of circulating fluid, neurogenic dysfunction and adrenal exhaustion. Section III discusses blood changes in shock, Section IV, in discussing potassium, gives elaborate tables of lethal doses and seven pages of electrocardiograms in the experimental animal, Section V is entitled 'The Historical Treatment of Shock'—meaning presumably the history of the treatment of shock. The next four sections deal briefly with physical measures of hemoconcentration, experimental shock, normal and abnormal blood values in the human subject and limiting factors in potassium analysis. Section X, although entitled 'Advances in the Treatment of Shock' treats solely the use of the adrenocortical hormone, which is disposed of in five paragraphs, notwithstanding its importance as the author's main theme.

Sections XI and XII give adequate protocols of a number of cases illustrating various types of shock. The reader notes with interest the treatment followed which in most cases includes the standard and the newer methods, and he may or may not agree with the author's enthusiasm for the use of the adrenocortical hormone. Section XIV,

entitled "Historical Development in the Conception and Treatment of Shock," lists two hundred and twenty-nine names and endeavors, in a brief sentence or two, to indicate the part played by each: for example, "Cannon, 1923, against adrenal glands in shock." Sections XV and XVI attempt to cover, respectively, in the same way, "The Physiologic and Toxicologic Effects of Potassium" and "Some of the Functions of the Adrenal Glands." Section XVII, which is a bibliography of five hundred and thirty-three references, is followed by author and subject indexes and a useful ten-page laboratory manual.

The volume is a sumptuous one characterized by lavishness in paper, illustrations, charts and symbolic graphs. Many pages contain but a short paragraph or a small chart. There are thirty blank pages for personal notes by the reader. Three beautiful full-page colored illustrations of test tubes, flasks and the normal adrenal gland add nothing that could not be satisfactorily dealt with by a few lines of text. In general, the author presents a wealth of brief citation without the all-essential critical evaluation and integration that would add so much to its value.

In clinical problems, the success of treatment is often proportional to the exactitude of available data in diagnosis. Dr. Scudder does well to remind the reader that the pulse rate and quality, the blood pressures, the blood count and the hemoglobin estimation are occasionally misleading and that the hematocrit, the specific gravity of blood and plasma and the level of plasma proteins add important evidence of hemoconcentration and diminished effective blood volume, which may permit suspicion of impending shock before other evidence exists. In spite of his assurances of the simplicity and ease of these determinations, one cannot help believing that they may add difficulty, delay and even confusion in a situation demanding prompt action. The reviewer believes that in most cases the experienced surgeon who first shrewdly evaluates the facts and circumstances of the trauma and then considers the patient as a whole will rarely have difficulty in diagnosing impending or existing shock, and will meet all indications for treatment if he adopts the almost universally accepted simple methods, including the creation and maintenance of an effective blood volume by the introduction of blood, plasma or, sometimes, other fluids that will remain in the vascular channels.

*The Successful Error: A critical study of Freudian psychoanalysis.* By Rudolf Allers, M.D., Ph.D. 8°, cloth, 266 pp. New York: Sheed and Ward, Incorporated, 1940. \$3.00.

This is a useful book for those who wish to formulate their negative and critical reactions to psychoanalysis, and to those who have these feelings and wish to find them well expressed. Psychoanalysis is most actively promulgated by those who believe in it and those to whom it is a religion. They zealously defend it, but just as psychoanalysis has its adherents, it also has its critics, and Dr. Allers is one of these. The psychoanalyst will say that Dr. Allers does not understand psychoanalysis and that he is biased, hence not qualified to criticize it. In reading the book, one gets the impression that he has tried consciously to be objective, and certainly his criticism is based on his own philosophic and scientific training, which appears to be dignified. Dr. Allers has a medical background and training, and is probably better versed in the use of logic than most psychoanalysts. For these reasons and because his book is a thoughtful and sincere document, it is worth reading. Whatever the future may bring to prove the "rightness" or "wrongness" of psycho-

analysis, this book will stand as one of the systematic and logical objections to numerous excessive claims for the therapeutic system with which Dr. Allers deals in detail.

One of the best chapters is on the subject of psychoanalysis and medicine. It is too complicated to summarize, but any physician, whether he is a psychoanalyst or not, will find that chapter interesting. If the reader is a psychoanalyst, he will probably find it very irritating.

This is not just another aimless dig or jab at psychoanalysis. It is a carefully leveled, well-aimed thrust.

*Medical Progress: Annual, 1940.* A series of fifty-two reports published during 1940 in the *New England Journal of Medicine*. Managing Editor: Robert N. Nye, M.D. 8°, cloth, 625 pp. Springfield, Illinois: Charles C Thomas, 1941. \$4.00.

Each week in the *New England Journal of Medicine*, there appears a critical review of a definite subject by a man well qualified to evaluate the current progress in the field. These reviews are usually more than a mere report on the current literature, for they discuss the problems in general, particularly in relation to recent advances. The fifty-two articles published in 1940 have now been collected into a volume of great value to medical students, practitioners and specialists alike. The quality of the articles is extremely high, and the reviewer knows of no other annual publication that sets a finer standard. The papers are clearly written, and although they are scientifically accurate and often detailed in their exposition of the subject, the material is presented in such a way that the ordinary practitioner may read it with understanding. The articles contain bibliographies. The book should receive the widest recognition, and it is difficult to conceive of any doctor in the practice of medicine who would not improve his practice by reading part or all of this volume. For the specialist, moreover, who desires to keep up in fields other than his own, this book offers an invaluable opportunity. In addition, the book should be compulsory reading for all third-year and fourth-year medical students.

*Necropsy: A guide for students of anatomic pathology.* By Béla Halpert, M.D. 12°, cloth, 75 pp. St. Louis: The C. V. Mosby Company, 1941. \$1.50.

This small book describes the autopsy technic practiced by Ghon and adopted by the author. The descriptions of technic are not always adequate because of the lack of illustrations. Its principal value lies in the suggestions of possible pathological findings in the various systems of the body.

## NOTICES

### MASSACHUSETTS MEDICAL BENEVOLENT SOCIETY

The annual meeting of the Massachusetts Medical Benevolent Society will be held at the Boston Medical Library on Monday, October 27, at 5:15 p.m. A meeting of the council will be held at 5 p.m.

### MASSACHUSETTS MEMORIAL HOSPITALS

The regular staff meetings of the Massachusetts Memorial Hospitals will be held in the Evans Memorial Auditorium at 8:15 p.m. on October 31, January 2, February 27 and April 24. Dr. Chester S. Keefer will be the chairman. At the first meeting, Dr. Joseph F. Ross will speak on "The Metabolism of Radioactive Iron."

## MASSACHUSETTS GENERAL HOSPITAL

The clinical staff meetings of the Children's Medical Service of the Massachusetts General Hospital were resumed on Friday, October 17, in the Ether Dome at 12 m. Subsequent meetings will be held on the following Fridays: October 31, November 14 and 28, December 12, and January 2, 16, and 30

## ROBERT BRECK BRIGHAM HOSPITAL

Dr. Carl C. Seltzer will speak on "Anthropometry and Arthritis: Difference between rheumatoid and degenerative joint diseases, males and females" at the Robert Breck Brigham Hospital on Monday, October 27, at 8 p.m. Drs. E. A. Hooten and Walter Bauer will lead the discussion.

Physicians and medical students are cordially invited

## PORTSMOUTH NAVAL HOSPITAL

There will be a meeting of the staff of the United States Naval Hospital, Portsmouth, New Hampshire, on Tuesday, November 4, at 8 p.m. Dr. Merrill Moore, of Boston, will speak on "Alcoholism: Its cause and treatment."

The members of the local societies in and about Portsmouth are cordially invited to attend

## SOCIETY MEETINGS AND CONFERENCES

## CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, OCTOBER 26

## MONDAY, OCTOBER 27

- 11:15-1:15 p.m. Clinicopathological conference Peter Bent Brigham Hospital amphitheater
- 5:00 p.m. Massachusetts Medical Benevolent Society Boston Medical Library, 8 Fenway
- 8 p.m. Anthropometry and Arthritis: Difference between rheumatoid and degenerative joint diseases, males and females Dr. Carl C. Seltzer Robert Breck Brigham Hospital

## TUESDAY, OCTOBER 28

- 9:00-10:00 a.m. Medical clinic Dr. S. J. Thannhauser Joseph H. Pratt Diagnostic Hospital
- 11:15-1:15 p.m. Clinicopathological conference Peter Bent Brigham Hospital amphitheater
- 5:00 p.m. The Chemical Reactions of the Body Fats Prepared by Dr. Rudolf Schoenheimer and delivered by Professor Hans T. Clarke Edward A. Dunham Lecture Harvard Medical School amphitheater, Building C
- 8:00 p.m. Massachusetts Society of X-Ray Technicians Inc. New England Baptist Hospital

## WEDNESDAY, OCTOBER 29

- New England Postgraduate Assembly Sanders Theatre Harvard University, Cambridge
- 9:00-10:00 a.m. X-ray Demonstration Or Alice Einstein Joseph H. Pratt Diagnostic Hospital
- 12:00 m. Clinicopathological conference Children's Hospital
- 5:00 p.m. The Chemical Reactions of the Body Proteins Prepared by Dr. Rudolf Schoenheimer and delivered by Professor Hans T. Clarke Edward A. Dunham Lecture Harvard Medical School amphitheater, Building C
- 7:00 p.m. Neisserian Medical Society of Massachusetts Hotel Kenmore, Boston

## THURSDAY, OCTOBER 30

- New England Postgraduate Assembly Sanders Theatre Harvard University, Cambridge
- 8:30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital at the Children's Hospital Conducted by Dr. F. R. Ober
- 9:00-10:00 a.m. Medical clinic Or S. J. Thannhauser Joseph H. Pratt Diagnostic Hospital
- 3:00-6:00 and 7:00 p.m. Massachusetts Public Health Association Commander Hotel Cambridge
- 5:00 p.m. The Dynamic State of the Body Constituents Prepared by Dr. Rudolf Schoenheimer and delivered by Professor Hans T. Clarke Edward A. Dunham Lecture Harvard Medical School amphitheater, Building C

8:00 p.m. Some Local Uses of Estrogenic Hormones in Obstetrics and Gynecology Dr. Norris W. Vaux Journal Club meeting, Boston Lying in Hospital

## FRIDAY, OCTOBER 31

- 9:00-10:00 a.m. The Differential Diagnosis of Hemoglobinuria Dr. T. Hale Ham Joseph H. Pratt Diagnostic Hospital
- 12 m. Clinical staff meeting of the Children's Medical Service Massachusetts General Hospital Ether Dome
- 8:15 p.m. The Metabolism of Radioactive Iron Joseph F. Ross Massachusetts Memorial Hospital

## SATURDAY, NOVEMBER 1

- 9:00-10:00 a.m. Presentation with discussion dispensary and district cases Joseph H. Pratt Diagnostic Hospital
- \*Open to the medical profession

OCTOBER 29-NOVEMBER 1 Association of Military Surgeons Page 473 issue of September 18

OCTOBER 31-JANUARY 30 Massachusetts General Hospital Clinical staff meetings of the Children's Medical Service Notice above

OCTOBER 31-APRIL 24 Massachusetts Memorial Hospitals Staff meetings Page 672

NOVEMBER 3-7 American College of Surgeons Page vii issue of July 31

NOVEMBER 4 Portsmouth Naval Hospital Notice above

NOVEMBER 5-6 American Conference on Industrial Health Page 473, issue of September 18

NOVEMBER 13 Pentucket Association of Physicians

NOVEMBER 17-19, 21-22, 27 and 30 Thomas William Salmon Memorial Lectures Page 616, issue of October 16

JANUARY 3 American Board of Obstetrics and Gynecology Page 473 issue of September 18

JANUARY 10-11 Forum on Allergy Page 392, issue of September 4

APRIL 6-10 American Congress on Obstetrics and Gynecology Page 600 issue of October 9

APRIL 20-24 American College of Physicians Page 996, issue of June 5

## DISTRICT MEDICAL SOCIETIES

## BIRKSHIRE

OCTOBER 30  
APRIL 30

## BRISTOL, NORTH

APRIL 16 Taunton

## ESSEX, NORTH

JANUARY 7 Haverhill  
MAY 6 Lawrence

## ESSEX, SOUTH

NOVEMBER 12 Beverly Hospital Beverly  
DECEMBER 3 Salem Hospital Salem  
JANUARY 7 Danvers State Hospital, Hathorne  
FEBRUARY 11 Lynn Hospital, Lynn  
MARCH 4 Essex Sanatorium Middleton  
APRIL 1 Addison Gilbert Hospital Gloucester  
MAY 13 Annual meeting (place to be announced)

## FRANKLIN

NOVEMBER 11  
JANUARY 13  
MARCH 10  
MAY 12 Annual meeting

Meetings will be held at the Franklin County Hospital at 11:00 a.m.

## HAMPSHIRE

NOVEMBER 5 Veterans Hospital, Leeds 4:30 and 6:00 p.m.  
JANUARY 7 Belchertown State Hospital, 1:00 and 4:00 p.m.  
MARCH 4 Hotel Northampton Northampton, 4:30 and 6:30 p.m.  
MAY 6 Hotel Northampton Northampton 8:30 p.m.

## MIDDLESEX, EAST

NOVEMBER 12  
JANUARY 28  
MARCH 18  
MAY 6

All meetings will be held at 12:15 p.m. at the Bear Hill Golf Club Stoneham, except that of May 6, which will be held at Woburn at 6:30 p.m.

## MIDDLESEX, NORTH

OCTOBER 29  
JANUARY 28  
APRIL 29

## NORFOLK

OCTOBER 28.  
 NOVEMBER 25.  
 JANUARY 27.  
 FEBRUARY 24.  
 MARCH 24.  
 MAY 1-15 (date to be announced).

All meetings will be held at the Hotel Sheraton, Boston, except that of October 28, which will be held at the Marine Hospital, Brighton.

## NORFOLK SOUTH

NOVEMBER 6.  
 DECEMBER 4.  
 JANUARY 8.  
 FEBRUARY 5.  
 MARCH 5.  
 APRIL 2.  
 MAY 7.

All meetings will be held at 12.00 noon at the Norfolk County Hospital, South Braintree, with the exception of that of February 5, which will be held at the Quincy City Hospital, Quincy.

## PLYMOUTH

NOVEMBER 20, Plymouth County Hospital, South Hanson  
 JANUARY 15 Brockton Hospital, Brockton.  
 FEBRUARY 19, Jordan Hospital, Plymouth.  
 MARCH 19 Goddard Hospital, Brockton.  
 APRIL 16 Bridgewater State Farm, Bridgewater.  
 MAY 21 Lakeville Sanatorium, Middleboro

## SUFFOLK

APRIL 29 Annual meeting. 8 15 p.m., Boston Medical Library.

## WORCESTER

NOVEMBER 12 Grafton State Hospital, North Grafton  
 DECEMBER 10 Worcester City Hospital, Worcester  
 JANUARY 14 St Vincent Hospital, Worcester.  
 FEBRUARY 11, Worcester State Hospital, Worcester  
 MARCH 11, Memorial Hospital, Worcester.  
 APRIL 8, Hahnemann Hospital, Worcester.  
 MAY 13, Annual meeting, Worcester Country Club, Worcester

## WORCESTER NORTH

JANUARY 28, Leominster Hospital, Leominster  
 APRIL 22 Burbank Hospital, Fitchburg.  
 JULY 22 Henry Heywood Memorial Hospital, Gardner

## BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

*Trauma and Disease.* Edited by Leopold Brahdy, M.D., physician in charge of occupational diseases and injuries in the Office of the Corporation Counsel of the City of New York, and lecturer in radiology, New York University Medical School; and Samuel Kahn, M.D., medical examiner in the Bureau of Workmen's Compensation of the Department of Labor, State of New York. Second edition. 8°, cloth, 655 pp., with 13 illustrations and 13 tables. Philadelphia: Lea and Febiger, 1941. \$7.50.

*The Furtherance of Medical Research.* By Alan Gregg, M.D., director for the medical sciences, Rockefeller Institute. 8°, cloth, 129 pp. New Haven: Yale University Press, 1941. \$2.00.

*Leaders of Medicine: Biographical sketches of outstanding American and European physicians.* By Solomon R. Kagan, M.D. 8°, cloth, 176 pp., with 4 illustrations. Boston: The Medico-Historical Press, 1941. \$3.00.

*The Foot and Ankle: Their injuries, diseases, deformities, and disabilities, with special application to military practice.* By Philip Lewin, M.D., associate professor of bone and joint surgery, Northwestern University Medical School professor of orthopedic surgery, Post-Graduate Medical School of Cook County Hospital, attending orthopedic surgeon, Cook County Hospital, attending orthopedic surgeon, Michael Reese Hospital, Chicago, and consulting orthopedic surgeon, Municipal Contagious Disease Hospital, Chicago. Second edition. 8°, cloth, 665 pp. with 304 illustrations. Philadelphia: Lea and Febiger, 1941. \$9.00.

*Nostradamus: The man who saw through time.* By L. McCann. 8°, cloth, 421 pp. New York: Creative Art Press, Incorporated, 1941. \$2.75.

*The New International Clinics: Original contributions, clinics, and evaluated reviews of current advances in medical arts.* Edited by George Morris Piersol, M.D., professor of medicine, Graduate School of Medicine, University of Pennsylvania, Philadelphia. Vol. III, N. S. 4, 15 8°, cloth, 300 pp. Philadelphia: J. B. Lippincott Company, 1941. \$3.00.

*The Roentgen Density of the Cystine Calculus: A roentgenographic and experimental study, including a comparison with more common uroliths.* By Axel Renan. Translated from the Swedish by Catherine Djurklou. paper, 148 pp., with 67 illustrations and 23 tables. Stockholm: P. A. Norstedt and Sons, 1941. 15 Sw. Cr.

*Essentials of General Surgery.* By Wallace P. Ritt, M.D., clinical assistant professor, Department of Surgery, University of Minnesota Medical School. 8°, cloth, pp., with 237 illustrations. St. Louis: The C. V. Mosby Company, 1941. \$8.50.

*Bibliographia primatologica: A classified bibliography of primates other than man.* Part I: Anatomy, embryology and quantitative morphology; physiology, pharmacology and psychobiology; primate phylogeny and miscellanea. By Theodore C. Ruch, B.Sc., Ph.D., Yale University School of Medicine. With an introduction by John F. Flannery, B.S., A.M., Ph.D., Yale University School of Medicine. 4°, cloth, 241 pp. Springfield, Illinois: Charles C. Thomas, 1941. \$8.50.

*Sulfanilamide and Related Compounds in General Practice.* By Wesley W. Spink, M.D., associate professor of medicine, University of Minnesota Medical School. cloth, 256 pp. Chicago: The Year Book Publisher, Incorporated, 1941. \$3.00.

*Society and Medical Progress.* By Bernhard J. Stern. cloth, 264 pp. Princeton: Princeton University Press, 1941. \$3.00.

*A Manual of Bandaging, Strapping and Splinting.* Augustus Thorndike, Jr., M.D., associate in surgery, Harvard Medical School, and surgeon to the Department of Hygiene, Harvard University. 16°, paper, 144 pp., 117 illustrations. Philadelphia: Lea and Febiger, 1941. \$1.50.

*Beiträge zur Röntgendiagnostik: Der Otitis Media und ihrer Komplikationen im Schlafenden.* By

(Continued on page x)

# The New England Journal of Medicine

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## LIVER DOSAGE IN PERNICIOUS ANEMIA\*

### Failure of Quantitative Storage of Hematopoietic Principle

WILLIAM B. SEYMOUR, MD,† ROBERT W. HEINLE, MD,† AND  
FRANKLIN R. MILLER, MD,‡

CLEVELAND

**T**REATMENT of patients with pernicious anemia by parenteral liver extract has become such a well established procedure that it needs no further discussion. The usual method involves the administration of conveniently sized doses of liver extract at regular intervals of one, two, three and, occasionally, four weeks. The size of each dose and the interval between treatments must be regulated by the requirements of the patient as determined by observation in each case.

Normal persons manufacture the hematopoietic principle effective in pernicious anemia by the interaction of intrinsic (gastric) factor and extrinsic (food) factor.<sup>1</sup> This reaction presumably takes place in the intestinal tract,<sup>2</sup> and the product of the interaction is recovered from the liver in the preparation of the liver extracts effective in the treatment of pernicious anemia. It has been thought that the liver might be a storehouse for the hematopoietic principle,<sup>3-6</sup> and that its only function is to release this principle as the necessity arises. If it were possible for the liver to store the hematopoietic principle quantitatively without any excretion or destruction, it is conceivable that large amounts of liver extract might be administered over a short period to patients with pernicious anemia and thus enable them to remain in remission as long as if the same total dose of liver extract were given in the usual manner of smaller doses at regular, frequent intervals. Miller,<sup>7</sup> in 1936, suggested this possibility and presented data showing that some such storage might take place. Strauss and Pohle<sup>8</sup> sub-

sequently presented similar data indicating that, although some storage may take place, patients with pernicious anemia generally do not remain in remission so long when treated with single massive doses as when they receive the same total dose in smaller amounts at spaced intervals.

The observations reported here were made on 9 patients with pernicious anemia in remission and 13 patients with pernicious anemia in relapse. Six were men, and 16 were women. All had been observed at some previous time during both relapse and remission. The 9 patients in remission had been followed previously for ten to forty-six weeks during remission; during this time they received doses of liver extract at intervals of two or three weeks, and the individual requirement was ascertained. The 13 patients in relapse had also been followed from ten to forty-six weeks during a remission, so that their individual maintenance dosage of liver extract was similarly established. Subsequently, these 13 patients failed to keep scheduled appointments for treatment, so that when next seen they were in relapse, at which time the observations reported here were begun.

For purposes of discussion, patients were arbitrarily considered to be in remission when the red cell count was 4,000,000 or more, with a hemoglobin of 90 per cent (14.0 gm per 100 cc.). Values less than these constituted a relapse. All patients had typical Addisonian pernicious anemia, including the usual blood findings, absence of free hydrochloric acid after subcutaneous administration of histamine and varying degrees of posterolateral column sclerosis. All had been seen in relapse at least once before the beginning of this study, and all had responded to liver extract or oral stomach preparations in the expected manner.

Figure 1 shows the results when the 9 patients

\*From the H. K. Cushing Laboratory of Experimental Medicine, Department of Medicine, Western Reserve University, and the Medical Service, Lakeside Hospital.

†Instructor in Medicine, Western Reserve University physician, University Hospitals of Cleveland.

‡Formerly assistant professor of medicine, Western Reserve University physician, University Hospitals of Cleveland.

in remission were treated with massive doses of liver extract. These patients received 55 to 140 U.S.P. units of parenteral liver extract<sup>9</sup> in ten to thirty days' time, after which no liver or liver extract was given until the blood showed evidence

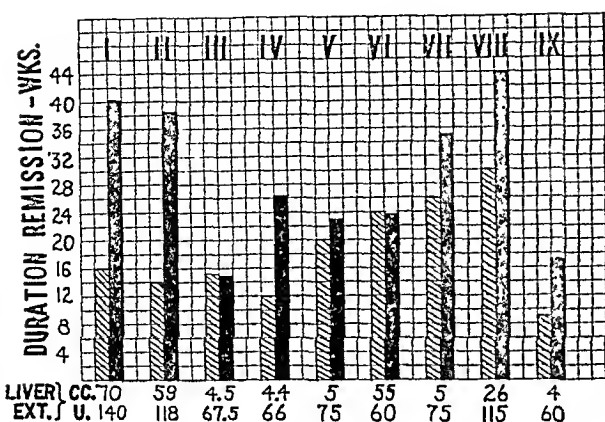


FIGURE 1. Patients with Pernicious Anemia in Remission.

The actual durations of remission (cross-hatched areas) following massive doses of liver extract are compared with the calculated durations of remission (solid areas) that would have obtained if the same amount of liver extract had been given in the usual intermittent doses.

of relapse as previously defined. In Figure 1, the cross-hatched bars represent the actual length of time the patients remained in remission following the massive liver treatment; the solid bars represent the calculated length of time the patients would have remained in remission had the same total dose of liver extract been administered in smaller amounts spaced at regular intervals of two or three weeks. In all but 3 of the 9 cases, relapses occurred much sooner with massive-dose therapy than they would have occurred with the intermittent-dose method. In Cases 3, 5 and 6, the interval of remission was about the same. The explanation of why these 3 cases were apparently able to store the liver extract quantitatively will be considered subsequently.

It must be mentioned, at this point, that there may have been some error in determining the actual maintenance dose of liver extract required by these patients when they were treated in remission with the usual small, intermittent doses. An effort was made to give the patients just enough liver extract to cause them to remain in remission. However, it is probable that a somewhat greater amount was given than was actually required, since none of the patients were allowed to relapse during the period of maintenance observation. Even though this factor caused the results of massive dose treatment to appear more favorable, they are generally not so good as those

which would have been obtained had the same total dose of liver extract been given in small, regular, intermittent doses. Table 1 shows the volume and number of units of liver extract utilized per week in both the massive-dose and intermittent-dose methods of treatment.

It can also be seen from Table 1, by comparing doses in cubic centimeters with the units contained, that both crude and concentrated liver

TABLE 1. Volume and Units of Liver Extract Utilized per Week by Patients with Pernicious Anemia in Remission, Using Massive-Dose and Intermittent-Dose Therapy.

CASE No.	LIVER EXTRACT UTILIZED PER WEEK			
	MASSIVE DOSE		INTERMITTENT DOSE	
	cc.	units	cc.	units
1	4.37	8.74	1.74	3.48
2	4.21	8.42	1.53	3.06
3	0.30	4.50	2.30	4.60
4	0.37	5.50	2.50	2.50
5	0.25	3.75	0.18	3.26
6	2.08	2.08	2.10	2.10
7	0.84	3.71	1.31	2.62
8	0.44	6.66	1.74	3.48
9	0.19	2.88	2.10	2.10

extracts were employed in the study of these patients. We do not wish to discuss the relative merits of these two types at this time and only call attention to the fact that, so far as maintenance of blood levels is concerned, one type was as effective as the other.

The results when massive doses of liver extract were given to patients in relapse are shown in Table 2. In these cases, the duration of the actual

TABLE 2. Attainment and Maintenance of Remission by Patients with Pernicious Anemia in Relapse After Treatment with Massive Doses of Liver Extract Given in Ten to Thirty Days.

CASE No.	RED-CELL COUNT* X 10 <sup>6</sup>	HEMOGLOBIN† %	LIVER EXTRACT		DURATION OF REMISSION weeks
			cc.	units	
10	1.30	38	130	260	17
11	1.70	50	165	330	17
12	2.10	62	80	160	19
13	0.60	24	70	140	15
14	1.50	53	190	380	22
15	3.20	87	115	230	13
16	3.50	92	85	185	13
17	3.60	76	80	160	17
18	3.80	65	50	100	16
19	3.30	70	60	120	29
20	2.60	60	45	90	16
21	1.20	32	120	240	13
22	3.90	80	70	140	

\*At beginning of treatment.

†100 per cent hemoglobin = 15.6 gm. per 100 cc.

remission cannot be compared with that which would have resulted if treatment had been instituted during remission, since there is no method of calculating how much liver extract these patients utilized before remission was attained. These 13 patients were given 90 to 380 units of liver ex-



tract intramuscularly in ten to thirty days. A maximal reticulocyte response and a rapid increase in red blood cells and hemoglobin occurred in each case. It is evident that these patients were able to attain and maintain remission for longer periods than if liver extract had been given in dosage sufficient only to produce a maximal reticulocyte response. All these patients attained remission blood levels and remained in remission for thirteen to twenty-nine weeks without further treatment of any sort.

As previously noted from Figure 1 and Table 2, there is considerable variation in a patient's ability to store liver extract. The most reasonable explanation of this depends on the fact that pernicious anemia is the result of a relative and not necessarily an absolute deficiency of gastric intrinsic factor. Goldhamer<sup>10</sup> has shown that patients with pernicious anemia have some intrinsic factor in their stomachs, although it is obviously not present in sufficient quantities to prevent the occurrence of anemia. If gastric juice is removed daily from certain of these patients, pooled until large quantities are obtained, and administered to the same or other patients with pernicious anemia in relapse, a hematopoietic response ensues, similar to that produced with normal gastric juice and indicating that some intrinsic factor is present.

It is reasonable to assume, therefore, that there are all degrees of pernicious anemia from mild to severe, depending on the degree of deficiency of intrinsic factor. The patients with mild cases, although they do not manufacture enough hematopoietic principle to prevent anemia, obviously manufacture more hematopoietic principle than those with severe cases and, hence, greater deficiencies, and the former need less liver extract than the latter.

To test this hypothesis, we selected 2 patients who had mild pernicious anemia as evidenced by

eral months by the daily feeding of whole liver. At the beginning of the observation period shown in Table 3, all liver and stomach products were removed from the diet, and 120 gm. of beef or two eggs daily were added—both beef and eggs are known to be good sources of extrinsic factor.<sup>11</sup> On this regimen, the patient remained in remission for a period of thirty-nine weeks, although no specific therapy was administered. At the end of this period, she was unwilling to follow the diet longer, and therapy with liver was resumed.

The second patient, C. R., in addition to pernicious anemia, had hypertension and angina pectoris. Twenty-eight weeks preceding the observation period recorded in Table 4, the patient re-

TABLE 4. Data on Patient C. R.

PERIOD OF OBSERVATION weeks	THERAPY*	RED CELL COUNT × 10 <sup>6</sup>	HEMOGLOBIN %
0	60 to 120 gm beef or 1 to 2 eggs daily	3.80	94
2	60 to 120 gm beef or 1 to 2 eggs daily	4.90	102
4	60 to 120 gm beef or 1 to 2 eggs daily	4.89	101
6	60 to 120 gm beef or 1 to 2 eggs daily	5.60	103
8	60 to 120 gm beef or 1 to 2 eggs daily	4.66	100
11	60 to 120 gm beef or 1 to 2 eggs daily	4.41	96
13	60 to 120 gm beef or 1 to 2 eggs daily	4.70	101
15	60 to 120 gm beef or 1 to 2 eggs daily	4.56	100
17	60 to 120 gm beef or 1 to 2 eggs daily	4.60	99
19	60 to 120 gm beef or 1 to 2 eggs daily	4.60	97
21	60 to 120 gm beef or 1 to 2 eggs daily	4.55	99
23	60 to 120 gm beef or 1 to 2 eggs daily	4.70	104
26	60 to 120 gm beef or 1 to 2 eggs daily	4.71	99
29	60 to 120 gm beef or 1 to 2 eggs daily	4.55	99
33	60 to 120 gm beef or 1 to 2 eggs daily	4.81	101
37	60 to 120 gm beef or 1 to 2 eggs daily	4.49	98
40	60 to 120 gm beef or 1 to 2 eggs daily	4.63	94
44	60 to 120 gm beef or 1 to 2 eggs daily	4.48	97
48	60 to 120 gm beef or 1 to 2 eggs daily	4.56	97
50	60 to 120 gm beef or 1 to 2 eggs daily	3.93	94
51	45 gm yeast daily	4.01	
53	45 gm yeast daily	4.02	89
55	45 gm yeast daily	4.49	98
57	5 units liver extract intramuscularly	3.70	89
61	60 to 120 gm beef or 1 to 2 eggs daily	4.71	93
65	60 to 120 gm beef or 1 to 2 eggs daily	4.49	89
69	10 units Camplin	3.90	92
73		4.49	90
77		4.35	89
81		4.27	87
85	22 units liver extract intramuscularly	3.85	80
89	20 units liver extract intramuscularly	3.91	85
93		4.90	97
97		4.26	84
101		4.99	97
105		4.45	93

\*Patient had received 10 units of liver extract intramuscularly twenty-eight weeks preceding the beginning of this period, no other antianemic substance given

TABLE 3. Data on Patient H. P.

DURATION OF TREATMENT*	RED-CELL COUNT × 10 <sup>6</sup>	HEMOGLOBIN %
weeks		
0	4.20	100
7	4.61	101
11	5.09	102
13	4.63	101
19	4.70	94
27	4.63	97
35	4.58	95
39	4.50	92

\*The diet included 120 gm of beef or two eggs daily. No liver or liver extract was administered during this period. Prior to this period the patient had maintained herself on whole liver by mouth.

the fact that they did not require so much liver or liver extract to maintain remission as the average case of pernicious anemia did. The first patient, H. P., had been kept in remission for sev-

ceived a single dose of 10 units (2 cc.) of liver extract intramuscularly. At the beginning of the period recorded, 60 to 120 gm. of beef or one to two eggs daily were added to the diet. The patient disliked both these foods and had not been eating either regularly. She remained in remission for fifty weeks, at the end of which she refused to include the items in her diet, and the blood showed a relapse. At this time, she was given 45 gm. of brewer's yeast daily. This material, which has a high protein content, is also an excellent source of extrinsic factor.<sup>12</sup> The blood showed improvement, but after six more weeks the patient

refused to ingest the yeast; another relapse occurred. She was given 5 units (1 cc.) of liver extract intramuscularly, with good results. At that time, she again started to eat beef or eggs, but because of her dislike for these foods, frequently omitted them from her diet. In spite of this, she received a total of only 52 units of liver extract intramuscularly during another forty-eight weeks. The patient decided that treatment should not be given so long as the red-cell count was over 4,000,000; this explains why the hemoglobin values were allowed to fall below 90 per cent (14.0 gm. per 100 cc.) on several occasions. When last seen, the patient felt perfectly well, showed no signs of progression of the posterolateral-column sclerosis, and had no complaints except frequent, mild attacks of angina pectoris.

There can be no doubt that these 2 patients represent true cases of pernicious anemia. Both were observed in severe relapse, and both reacted to liver with the usual reticulocyte response and increase in red-cell count and hemoglobin. Free gastric hydrochloric acid was absent in both after histamine was administered. The first patient had a moderate amount of posterolateral-column sclerosis. During subsequent periods of observation, it was found that even when these patients were given diets containing what is considered to be a normal amount of protein, an occasional dose of liver or liver extract was needed to maintain normal red-cell counts and hemoglobin levels. This is demonstrated in the last period of Table 4, but is not illustrated by the course of the first patient (Table 3), who has not been followed so regularly since the completion of the period shown.

It might reasonably be assumed that these two patients went into spontaneous remission coincident with the institution of the diet containing larger amounts of extrinsic factor, since it is well known that patients with pernicious anemia can undergo spontaneous remission lasting for months or even years. Although the explanation of such remissions has not been understood, it seems likely that either a spontaneous increase in gastric intrinsic factor or an increase of extrinsic factor in the diet might account for them. In the two cases described above, we believe that spontaneous remission occurred as a result of increasing extrinsic factor in the diet. It is probable that certain cases of spontaneous remission observed in the past resulted when patients, for one reason or another, increased the amount of extrinsic factor in the diet.

## DISCUSSION

It is unnecessary to assume any actual storage of hematopoietic principle to account for the fact that patients with pernicious anemia treated with massive doses of liver extract remain in remission for varying long periods. Regardless of the degree of deficiency of the gastric intrinsic factor, any patient can attain and maintain remission for some time after liver extract is given. The time that remission is maintained is longer in the patients with mild cases, who produce moderate amounts of hematopoietic principle, than it is in those with severe cases, who produce less hematopoietic principle.

The 2 cases maintained on extrinsic factor for long periods were sufficiently mild that only a small amount of extraneous hematopoietic principle was necessary to augment that made by the patients themselves. The fact that addition of extrinsic factor improves the formation of hematopoietic principle has been interpreted to be the result of a mass-action chemical phenomenon.<sup>12</sup> Since intrinsic factor added to extrinsic factor equals hematopoietic principle, increasing extrinsic factor causes an increase in the formation of hematopoietic principle, even though the intrinsic factor is present in less than normal amount.

Thus, the variation in amount of liver extract required by different patients is adequately explained. If the deficiency of intrinsic factor is relatively small and the amount of extrinsic factor in the diet is relatively large, less liver extract is necessary than if the reverse is true.

## SUMMARY AND CONCLUSIONS

Patients with pernicious anemia in remission given large doses of liver extract within a brief period remain in remission for varying periods. This time is generally not so long as that when the same total dose of liver extract is administered in small, intermittent doses.

Patients with pernicious anemia in relapse given large doses of liver extract in a short period attain and maintain remission for varying lengths of time without further treatment.

If hematopoietic factor is stored in the body, such storage is not quantitative when large doses of liver extract are administered in a short period. The fate of the unused hematopoietic principle is unknown.

By augmenting the extrinsic factor in the diet, two patients with mild pernicious anemia were maintained in remission for long periods without any specific treatment.

The degree of deficiency of intrinsic factor and the amount of extrinsic factor in the diet of patients with pernicious anemia probably account for the individual variation in requirements of liver extract.

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## CONTROLLED ADMINISTRATION OF FLUID IN SURGERY\*

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ROBERT Boyle,<sup>1</sup> the physicist, was interested in the density of many things. In 1683, while weighing blood and serum, he noted that in acute disease the specific gravity was higher and in chronic disease lower than normal. In the next century, Jurin<sup>2</sup> confirmed these observations. However, it was not until the nineteenth century that this knowledge was applied clinically. O'Shaughnessy<sup>3</sup> in England and Wittstock<sup>4</sup> in Germany demonstrated in 1831 that in Asiatic cholera the specific gravity of blood is considerably higher than normal.

Roy,<sup>5</sup> using a simplified method of obtaining the density of blood, showed by animal experimentation in 1884 that the blood becomes heavier in shock. This phenomenon occurs before any fall in blood pressure. Roy wished to find where the fluid lost from the blood could be found. By carrying out density determinations on the intestinal wall and on other organs, he showed that, in shock, fluid shifts from the blood into these tissues.

The first practical application of Roy's work was in India. Rogers,<sup>6</sup> the Surgeon General of India, considered the mortality in Asiatic cholera to be too high. In this disease, the patient goes into typical dehydration collapse due to vomiting, sweating and copious rice-water stools. A cold clammy skin, weak thready pulse, great mus-

cular weakness and marked prostration supervene. The only pulsating vessels are often the carotid arteries. The blood is viscid and thick, and the specific-gravity values of peripheral blood are often above 1.070. Besides hemoconcentration, there is a decrease in the sodium, an increase in the potassium concentration of the blood and a fall in the blood chloride and bicarbonate contents.

Both hypotonic and isotonic solutions had given disappointing results in cholera. Rogers introduced a slightly hypertonic (1.5 per cent) sodium chloride solution, and controlled the large administration of fluid by following the specific gravity of the peripheral blood. At times, as much as 10 to 12 liters was given within twenty-four hours before hemodilution was secured. Rogers issued an order that fluids should be stopped when the specific gravity of the blood reached 1.050. This was to prevent giving too much. This type of therapy reduced the mortality rate from Asiatic cholera at the Calcutta General Hospital from 59 per cent during the decade 1895-1905 to 26 per cent during the years 1910-1914.

The similarity between Asiatic cholera, intestinal obstruction and traumatic shock has often been noted. The chemical changes in the blood are identical.<sup>7</sup>

During World War I, Cannon<sup>8</sup> reported hemoconcentration in soldiers suffering from wound shock. Erythrocyte counts of 6,000,000 to 8,000,000 were associated with high mortality, especially if there was a great disproportion between the counts taken on capillary and those taken on venous blood. For some reason, this very im-

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portant observation is not widely known. Today, specific-gravity determinations are supplanting erythrocyte counts because of their far greater accuracy and sensitivity.<sup>9-11</sup>

The second test that is of value in assaying the degree of dehydration is the hematocrit or cell volume. During the early part of the nineteenth century, it was appreciated that in cholera the blood lost water. O'Shaughnessy<sup>3</sup> applied the term "crassamentum" to the solid matter that settled out on standing. In some cholera cases, the

can be determined within fifteen minutes, and afford accurate information about the state of the peripheral and venous circulating systems. They furnish data concerning the state of hydration. In cases of injury, changes of the specific gravity of capillary blood herald the approach of shock. One is thus forewarned and can institute therapy at a time when such corrective measures are most effective. These tests can differentiate shock due to internal blood loss from typical dehydration or traumatic shock before changes in blood pressure

TABLE 1. Blood Findings in a Patient with Multiple Injuries, including a Compound Fracture of the Tibia.

DATE	TIME	HEMATOCRIT	WHOLE BLOOD SPECIFIC GRAVITY	PLASMA SPECIFIC GRAVITY	PLASMA PROTEINS	PLASMA POTASSIUM	PLASMA SODIUM	PLASMA CHLORIDE	FLUID THERAPY
		%			gm / 100 cc	milliequiv / liter	milliequiv / liter	milliequiv / liter	
April 5	8 30 p.m. (admission)	44.9	1.0561	1.0293	7.62	3.6	141.6	105.8	Dried serum equal to 1500 cc., intravenously; 10 cc., by mouth
	10 30 p.m.		1.0503						
	12 00 midnight (end of operation)	30.6	1.0484	1.0255	6.33	4.1	142.2	105.0	
April 6	10 30 a.m.	35.3		1.0261	6.53	5.3	137.6	104.8	2700 cc., by mouth; 1000 cc., subcutaneously; 500 cc., transfusion
April 7									2950 cc., by mouth
April 8	9 00 a.m.	26.3		1.0256	6.36	3.6	131.2	100.0	2650 cc., by mouth
April 9									3200 cc., by mouth; 200 cc., transfusion
April 10	9 20 a.m.	29.1		1.0257	6.39				

water loss from the blood was so extreme as to leave only 27.5 per cent fluid and 72.5 per cent solids. This may be taken as the first objective measurement of decreased plasma volume in shock.

Blix<sup>12</sup> presented at Upsala the first *Haematokrit*. It was modeled after the *Laktokrit* used in the dairy industry. With this apparatus, Hedin<sup>13</sup> in 1891 reported values for normal men and women. In dehydration, whatever the cause, an increase in the hematocrit is characteristic.

The third test weighs a drop of plasma. This gives the total plasma solids and serves as another measure of dehydration.

The importance of the plasma proteins is now well recognized. One of their functions is protective. They also serve as a measure of dehydration. On account of the work of Weech and his associates,<sup>14</sup> one is able to compute the total plasma proteins from the specific gravity of the plasma. This is readily accomplished by using the modified Barbour and Hamilton apparatus<sup>7</sup> for the measurement of the specific gravities of body fluids.

These four values—the specific gravity of the peripheral blood, the hematocrit, the specific gravity of the plasma and the total protein content—

and before the appearance of the classic symptoms of shock.

In the postoperative care of the patient, the data furnished by these tests indicate whether blood should be administered; whether plasma and proteins should be used; whether salt solution is indicated; and, above all, when fluid therapy should be stopped. In addition to these helpful points, one can ascertain whether the fluid given is being utilized. In treating impending shock, should the blood become more concentrated after the administration of saline, one is immediately warned of the approach of a grave crisis. It is in just this state that the use of a potent adrenocortical hormone, along with salt, causes a reduction of hemoconcentration and a decrease in blood viscosity.

The restoration of blood volume in shock is essential. The restoration of blood volume with the proper type of fluid is even more important. In cases with renal failure or anuria, the flooding of the vascular system with intracellular water is poor therapy. For normal function, the differential salt concentration between the intracellular and extracellular compartments is necessary. Factors that upset this balance are harmful, in particular hypertonic solutions given in the dehydrated

state. Kidney function must be restored early in injury. The accumulation of intracellular salts in the blood plasma, due both to damage and to failure of excretion, tends to change the normal

state and was equivalent to 1500 cc. of liquid) was started intravenously, and the patient taken to the operating room for débridement and fixation of the fracture.

The cell volume and specific gravity of the peripheral blood were within normal limits (Table 1 and Fig. 1).

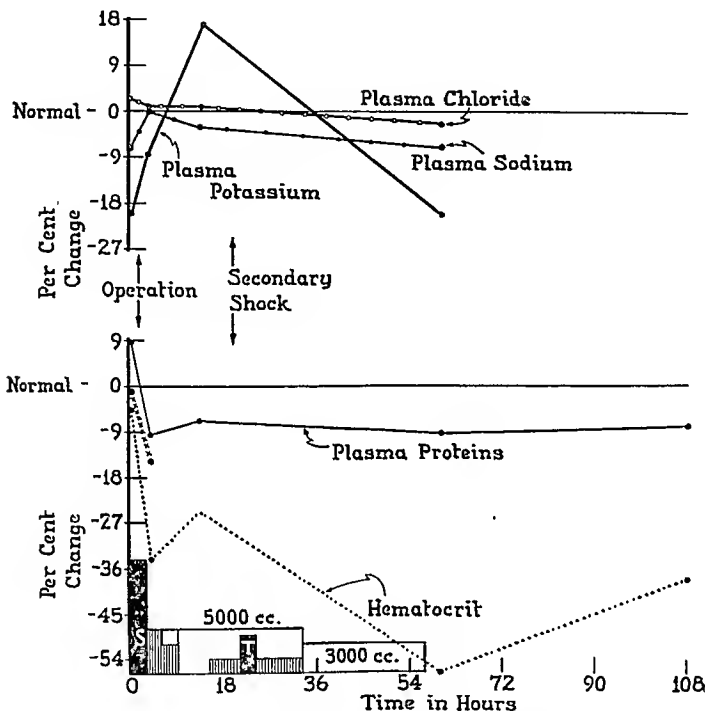


FIGURE 1. Traumatic Shock Due to an Automobile Accident: Multiple injuries, with compound fracture of the tibia.

ratio between intracellular potassium and extracellular sodium ions.

The following case of traumatic shock illustrates some of these points.

#### CASE REPORT

S. G. (P. H. 638287), a 59-year-old man, was brought to the hospital by ambulance a few minutes after an automobile accident in which he had sustained multiple contusions, lacerations and a compound fracture of the tibia. The patient was in primary shock, with a blood pressure of 80/60 and a pulse of 60. The leg had been fixed in a Thomas splint. The patient was conscious and oriented, but could not recall details of the accident.

He was given  $\frac{1}{4}$  gr. of morphine after blood had been secured for chemical studies and groupings. An infusion of serum (which had been reconstituted from the dried

The specific gravity of the plasma and the plasma proteins were elevated, findings that suggested a case of secondary anemia exhibiting hemoconcentration. The values of the sodium, potassium and chloride concentrations were not available at this time and illustrate that these determinations are valueless in directing emergency therapy on account of their time-consuming nature. They afford, however, valuable information about the effects of therapy when one reconsiders a case.

Blood dilution was secured with the serum, as shown by the falls in the hematocrit, specific gravity of capillary blood and plasma proteins. Eventually, there were decreases in the chloride and sodium concentrations, but the greatest change was a marked increase in the potassium concentration (from 3.6 to 5.3 milliequiv. per liter)<sup>15</sup> within 18 hours after the accident. Physiologic saline and Eschatin (adrenocortical extract) were withheld in the initial treatment because we wished to ascertain the effect

of serum alone on both the clinical and chemical aspects of shock.

On the following day, the patient went into typical secondary shock, which was combated with oxygen, infusions of physiologic saline and blood transfusion.

*Comment.* The administration of adrenocortical extract and salt during the initial treatment might have prevented the changes in sodium, potassium and chloride concentrations. The 58 per cent decrease in cell volume may have indicated overdilution of the blood, and points to the recommendation of giving 500 cc. of blood with every 500 cc. of plasma or serum, as recently advocated by Kekwick and his co-workers.<sup>16</sup>

### SUMMARY AND CONCLUSIONS

Four simple tests based on elementary physical chemistry are presented as a means of judging the state of hydration in the capillary and venous circulating systems. Their value lies in their simplicity, reproducibility and ease of mastery. Their practicability lies in the minimum amount of equipment necessary.

These tests are useful in shock, since they forewarn of its approach and hence allow early therapy. One case of shock is presented in which 1500 cc. of serum was used. The overdilution of the blood and the change in the electrolyte pat-

tern indicate that blood should have been given along with the serum and suggest that the administration of sodium and adrenocortical extract might have lessened the electrolyte changes.

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## PRIMARY CARCINOMA OF THE URETHRA IN THE MALE\*

### Report of a Case

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PRIMARY carcinoma of the urethra in the male is a comparatively rare disease. The first authentic case was reported in 1861 by Hutchinson.<sup>1</sup> In October, 1939, Kreutzmann and Coloff<sup>2</sup> searched the entire medical literature, and abstracted almost all the original case reports. With the addition of their own 2 cases, they brought the total of reported cases to 150. We report the following case because it serves well to illustrate the usual clinical course that this disease follows, the etiologic factors most commonly implicated and the diagnostic pitfalls most frequently encountered.

### CASE REPORT

A. L., a 58-year-old man, was admitted to the Lincoln Hospital on December 31, 1938. The patient had had some preliminary examination and treatment in another institution for the 2½ months directly preceding admission. Thirty-five years before hospitalization, he had had gonorrheal urethritis. He had no symptoms referable to the genitourinary tract until 5 years prior to entry, when he developed difficulty in starting the urinary stream,

some dribbling and occasionally a drop or two of bleeding at the end of micturition. This, associated with severe burning and urgency, made him seek treatment. He was seen at two hospital outpatient clinics, and was told that he had a urethral stricture. He was treated by numerous and repeated dilatations, and appeared to be peculiarly unresponsive to therapy. Each treatment was followed by severe pain and bleeding. The stricture did not seem dilatable. The patient was admitted to the wards of one of these first hospitals because of the fact that he had developed a markedly stammering urinary stream, frequency, nocturia and a urethral discharge. He had 200 cc. of turbid residual urine. X-ray studies of the kidneys, ureter and bladder showed no abnormalities. Cystoscopic examination revealed what appeared to be numerous strictures along the posterior urethra, moderate prostatic enlargement and generalized cystitis. It was believed that the patient's symptoms were largely due to the prostatic hypertrophy, and that they could be alleviated by prostatectomy. Hence, a bilateral vasectomy and suprapubic cystotomy were performed, in preparation for enucleation of the prostate. Ten days later, there was a profuse urethral discharge and marked perineal induration. With the appearance of a fluctuant mass, an incision was made in the perineum, and 200 cc. of foul pus was obtained. The perineal induration increased and spread, requiring repeated incisions and drainage. About a week before the patient entered Lincoln Hospital, it

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was found that sounds could not be passed into the bladder because of obstruction at the junction of the membranous and prostatic portions of the urethra. Nor could sounds be passed into the bladder through the perineal

Carcinoma of the urethra is a slowly progressive disease, affecting most frequently the membranous and bulbous portions of the urethra. Its

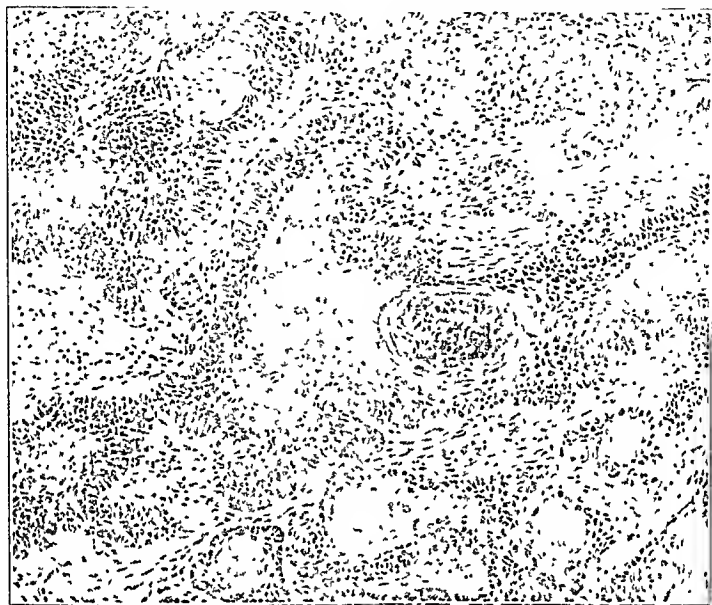


FIGURE 1. Typical *Acanthoma*, Showing Numerous Keratinizing Pearls

incisions. Fluid injected into the urethral meatus came through the perineal wounds.

On admission to Lincoln Hospital, the patient appeared acutely ill and cachectic. On January 26, 1939, after he had shown some improvement in his general condition, the perineum was completely exposed by enlarging the previous incisions. All necrotic tissue was removed, and the wound was irrigated and thoroughly packed. With increased drainage, the patient improved somewhat, but on February 14, because of extension of the infection in the perineum, the area was again incised. Suppuration involving the left ischiorectal fossa as high up as the left femoral triangle was found. There was marked sloughing of the bulbous and membranous urethra, with a urethroperineal fistula. The entire perineal area contained what seemed to be dense, cauliflowerlike inflammatory masses. Because of this appearance and the indolent healing, cancer was suspected, and a specimen removed for biopsy. Histologic examination of this tissue revealed that the mass was a typical squamous-cell epithelioma of the adult type (Fig 1), the commonest type of cancer of the urethra. X-ray examination of the pelvis, lumbar spine and long bones showed no evidence of metastases. There was no adenopathy.

The patient failed rapidly and expired about 1 month after this operation. Autopsy revealed that the membranous and bulbous portions of the urethra were entirely destroyed by a cauliflowerlike tumor (Fig 2), which extended throughout the entire length of these parts of the urethra.

recognition and course depend to some degree on the depth of the lesion in the urethra.

The initial symptoms of the disease are similar to and almost always mistaken for those of urethral stricture. However, suspicion should be aroused if presumable urethral strictures appear unresponsive to the usual treatment, or if perineal abscesses are intractable. Spread is by direct extension, with involvement of wide areas, which ultimately become necrotic and infected. Metastases are unusual, and regional adenopathy is most frequently due to infection. Distant metastasis is almost never seen, but when it does occur, the lung is the most frequent site.

The symptomatic course is divided into four stages by Kretschmer,<sup>3</sup> as follows: dysuria, retention and urethral discharge—the latter, if hemorrhagic, should lead one to suspect cancer; local tumor formation; periurethral infiltration with urine; and sinus formation. It is not until the latter two stages that carcinoma is suspected, so that diagnosis is generally late.

The etiology of urethral carcinoma, like that of all neoplastic disease, remains unknown. The

commonly held belief is that the condition is a metaplasia resulting from inflammatory irritation—in a large percentage of cases, gonorrheal urethritis is a common predecessor—or from re-

SUMMARY

A case of urethral carcinoma in the male is presented. The usual clinical course, the diagnostic pitfalls and the etiologic theories are illus-

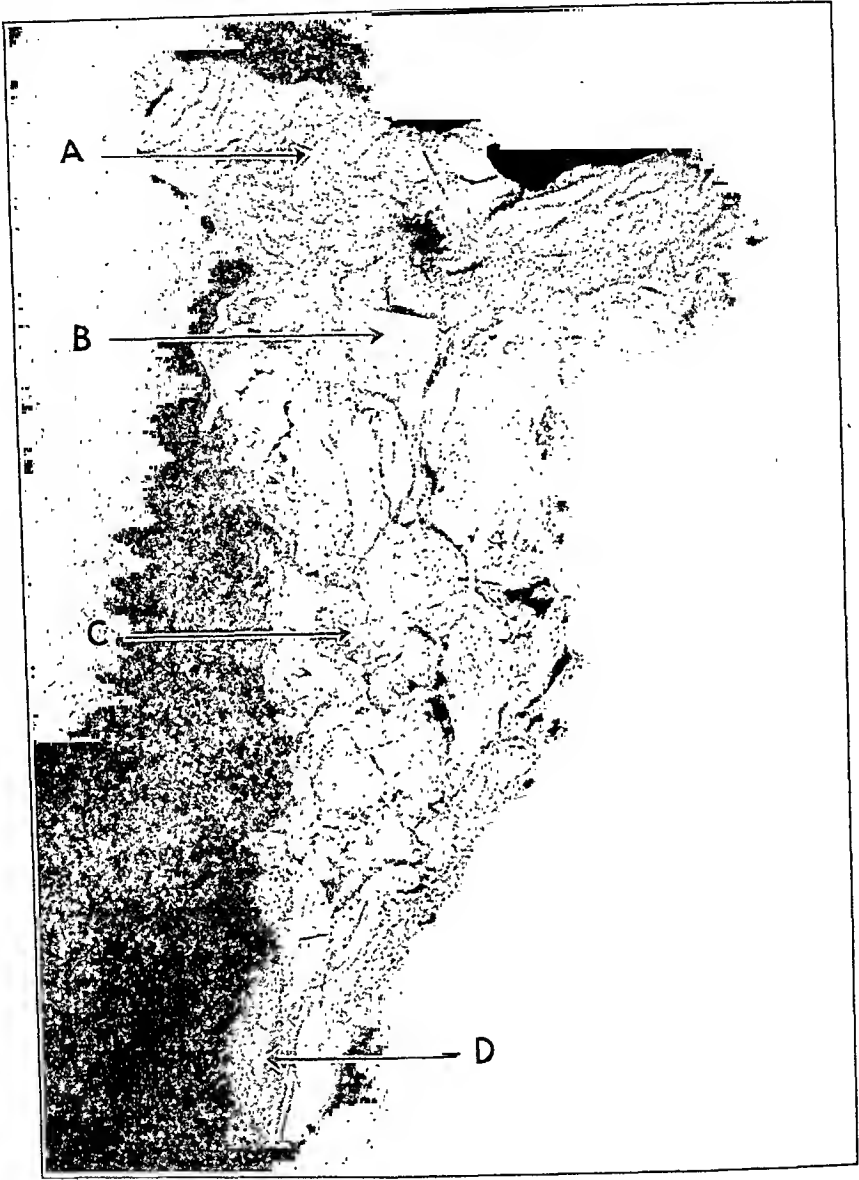


FIGURE 2. Gross Specimen Removed at Autopsy.

A—bladder; B—prostate; C—tumor mass, infiltrating and destroying the bulbous and membranous urethra; D—point of origin of tumor (about 2 cm. proximal to the glans).

peated trauma, such as that of repeated dilatations. Prognosis, which as a rule is very poor, can be improved only by early treatment. This necessitates early diagnosis. More frequent urethrocopies, with biopsy, in cases of intractable stricture, periurethral abscesses and sinuses that fail to heal, would increase the number of cases recognized. Treatment consists in either radical resection or deep x-ray therapy, or both.

trated and discussed. A plea is made for careful study, with biopsy, of intractable strictures, periurethral abscesses and sinuses that fail to heal, to facilitate early diagnosis and to improve the prognosis.

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## MENINGOCOCCEMIA WITHOUT MENINGITIS\*

## Report of a Case

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**M**ENINGOCOCCEMIA, as a disease entity, without meningitis or other complications, has been known only in the last forty years, the first case having been described by Salomon<sup>1</sup> in 1902. Since then, the disease has been widely reported.

Carbonell and Campbell<sup>2</sup> have defined and described the disease clearly and completely in their report of 3 cases, which, however, were treated with serum just at the dawn of sulfanilamide chemotherapy. Since sulfanilamide and its derivatives have been available, about a dozen cases thus treated have been reported, without a fatality; all were marked by prompt and complete recovery.

In 1937, Schwentker, Gelman and Long<sup>3</sup> reported briefly a case of uncomplicated meningococcemia in a series of meningococcal infections, which was successfully treated with sulfanilamide. Zende and Greenberg<sup>4</sup> reported an uncomplicated case in which the patient, ill three weeks when treatment was begun, recovered rapidly. Dimson,<sup>5</sup> in 1938, used pyridine (M & B. 693), with recovery in six days after the beginning of treatment. Craven,<sup>6</sup> in 1938, reported rapid clearing of all symptoms with complete recovery in a man ill with uncomplicated meningococcemia for seven weeks before treatment was begun. Long and Bliss<sup>7</sup> briefly mention "five cases suffering from acute meningococcemia without signs of meningitis in whom intensive therapy with the drug gave excellent curative results." Binns and Clancy,<sup>8</sup> in 1939, reported 2 additional cases much like the others: a child of twelve years ill for two months, and a forty-five year old man ill for seven weeks, before accurate diagnosis was made. Both patients rapidly recovered after sulfanilamide therapy was begun. Levy,<sup>9</sup> in 1937, treated a two year-old girl with both subcutaneous and oral therapy for nine days, with spectacular results. Kattwinkel<sup>10</sup> recently reported a case in which, with justification, the diagnosis of gonococcemia was originally made; the patient, a twenty two year-old woman, recovered rapidly following adequate oral doses of sulfanilamide. An additional case is reported below.

## CASE REPORT

A 55-year-old woman was admitted to the hospital on February 29, 1940, complaining of chills and fever, marula-

papular lesions on the face, trunk and extremities, and joint pains.

On February 15, 1940, the patient went to bed feeling quite well. She was awakened during the night with a marked chill. She took some aspirin and went back to sleep. The next morning, she felt fairly well, except for a mild sore throat and a stuffy feeling in her nose. At noon, she was nauseated, and vomited, with relief. The next day, February 17, however, she had another chill and developed high fever, and pain developed in many joints. She was given large doses of salicylates and bicarbonate of soda. The following day, a maculopapular rash was noted on both legs below the knees. Every 2nd or 3rd day from that time on, she developed a severe chill followed by high fever, varying between 103 and 105.4°F, each fastigium being followed by a fresh crop of maculopapular lesions, which gradually appeared over the entire body, accompanied by exacerbations of the polyarthralgia. No heat, redness or swelling appeared in any joints. During the remissions of fever, the patient became surprisingly well. Urinalysis was normal, the white-cell count was 12,800, with 82 per cent polymorphonuclears. A blood smear was negative for malaria. On February 29, 2 weeks after the onset, she agreed to hospitalization. The past history was negative for rheumatic heart disease, and was otherwise not pertinent.

On admission, the temperature was 99.2°F, the pulse rate 110, the respiratory rate 20, and the blood pressure 102/60. Physical examination revealed a fairly well nourished and well developed middle aged woman in no acute distress. The skin showed many reddish pink macules and papules over the entire body, predominately on the legs, some of which faded on pressure. One lesion on the left ankle was crusted. The lesions varied in size from several millimeters to 1 cm in diameter. The older lesions were brownish. The eyes reacted normally to light and accommodation. The fundi were normal. There was no stiffness of the neck. The lungs were clear. The heart rate was rapid, but there were no murmurs, thrills or enlargement. The abdomen was normal, except for skin lesions and an old surgical scar. There was slight inguinal adenopathy. Neurologic examination was entirely negative, including tests of the cranial nerves and the sensory and motor systems. All reflexes were active, and the Kernig, Brudzinski and Babinski signs were negative.

The red cell count was 3,800,000 with a hemoglobin of 72 per cent, and the white-cell count 12,900 with 85 per cent polymorphonuclears. There were slight poikilocytosis, anisochromia, polychromia, no erythroblasts and normal platelets. The clotting time was 1 minute, and the bleeding time 2 minutes and 15 seconds. The sedimentation rate (corrected) was 0.7 mm per min. The blood Hinton reaction was negative, the nonprotein nitrogen of the blood serum was 27 mg and the blood sugar 71 mg per 100 cc. Urinalysis showed the slightest possible trace of albumin and no sugar, with rare red and white blood cells in the sediment.

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Rheumatic fever, arthritic purpura, spotted fever, typhoid and undulant fever were considered, and blood was submitted to the laboratory. The patient meanwhile was given 60 to 90 gr. of salicylates daily, which controlled the joint pains quite well. These pains gradually subsided during the 1st week of hospital stay. On March 2, 4 and 6, the patient had further severe chills and high fever, new skin lesions following each attack.

Nose and throat cultures taken on March 7 were positive for *Micrococcus catarrhalis* on March 12. On March 7, the laboratory reported that the blood culture on February 29 showed meningococci, identified by sugar fermentations. The diagnosis was also checked by the Boston City Hospital laboratory. A second blood culture, taken March 7, was reported positive for meningococci on March 10.

Thirty grains (2.0 gm.) of sulfanilamide was given at once, followed by 20 gr. (1.3 gm.) every 4 hours. The blood sulfanilamide level was maintained between 11.8 and 14.3 mg. per 100 cc. from March 7 until March 15, although medication was reduced gradually from March 11 because of very rapid improvement. No further chills occurred, and the temperature never rose above normal after the beginning of sulfanilamide therapy; there were no further joint pains, and the skin lesions gradually disappeared. The white-cell count gradually dropped from 18,300 on March 5 to 10,000 on March 19. Two blood cultures, after sulfanilamide treatment had begun, were reported sterile. The patient received 905 gr. (60.3 gm.) of sulfanilamide, which she tolerated well, showing only moderate cyanosis. The drug was discontinued 13 days after therapy was begun. She was discharged from the hospital on March 23 without symptoms, 23 days after admission and 37 days after onset.

One year later, the patient was in excellent health.

## SUMMARY AND CONCLUSION

The literature on meningococcemia without meningitis is reviewed, and an additional case is reported. The diagnosis was obscure until verified by blood cultures in the third week of disease. All symptoms rapidly disappeared following sulfanilamide treatment.

The patients in the sulfonamide-treated cases of the disease thus far reported in the literature have all completely recovered promptly without sequelae.

Meningococcemia should be considered in any patient presenting symptoms of intermittent fever, unexplained rash and arthralgia.

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# MEDICAL PROGRESS

## NUTRITION\*

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THE purpose of this review is to emphasize, not the vitamins, — important though they are, — but the phase of nutrition that relates to national welfare, both present and future, and should be familiar to all physicians. In addition, several aspects of nutrition not commonly considered in reviews on deficiency disease are presented.

A rapidly increasing literature attests that the study of nutrition has passed the purely animal stage and is already deep into its application to human physiology and pathology. A number of the recent papers on this subject are purely inspirational and emphasize the lag between the accumulation and the practical application of nutritional knowledge.<sup>1-3</sup> Even the economic, social and political consequences that result from adequate or inadequate human nutrition are being considered.<sup>4-6</sup> World War II, with its mass experiments in malnutrition, and the defense efforts have stimulated an interest in nutrition never witnessed before in this country. Indeed, adequacy of nutrition may determine the political fate of a nation, as well as the physical well being and the morbidity and mortality of its people for a generation to come. The desire to have it favorably influence the Nation and the people becomes clearer each day.

### NATIONAL NUTRITION CONFERENCE FOR DEFENSE

The progress of nutrition in this country reached a pivotal point on May 26, 1941, when over eight hundred delegates (representing every interest in this field) met in Washington to attend the three-day National Nutrition Conference for Defense, called at President Roosevelt's request. The medical profession was well represented by noted nutritional authorities. Few such national conferences have been held, and none previously to discuss nutrition. Physicians may thus judge the import of this meeting. Procedures of the conference are not yet available, but a detailed review,<sup>7</sup> including parts of the original manuscripts, has been pub-

lished. Its scope is too vast for a complete analysis to be given. However, a few points will be presented so that its main objectives and far-reaching implications will be appreciated.

Brigadier General Lewis B. Hershey, deputy director of the Selective Service System, stated that, of 380,000 rejections for general military service, it had been estimated that perhaps one third were due either directly or indirectly to nutritional deficiencies. Paul V. McNutt, Federal Security Administrator, quoted President Roosevelt as emphasizing the present significance of the nutritional problem, as follows:

During these days of stress the health problems of the military and civilian population are inseparable. Total defense demands manpower. The full energy of every American is necessary. Medical authorities recognize completely that efficiency and stamina depend on proper food. Fighting men of our armed forces, workers in the industry, the families of these workers, every man and woman in America, must have nourishing food. If people are undernourished, they cannot be efficient in producing what we need in our unified drive for dynamic strength. . . . The Department of Agriculture has estimated that many millions of men, women, and children do not get the foods which science considers essential.

Surgeon General Thomas Parran summed up the American food situation in this way:

One half of our fuel — the calories we eat — is in the form of bread and sugar. Add to this the refined fats, and two thirds of our energy intake is in the form of "inert calories," which furnish fuel and nothing else. From the remaining third of our diet we must get the vitamin B complex and the minerals needed to burn up the inert calories. This is where we have been starving ourselves.

The Committee on Food Habits organized by the National Research Council will attempt by education and practical psychology to change the food habits of the public. Dr. Russell M. Wilder, chairman of the Committee on Foods and Nutrition, explained how the recent origin of scientific nutritional knowledge, the difficulty of recognizing minor clinical deficiencies and the prevalence of quackery and food fads in the nutritional field had made many physicians hesitate to apply the principles of nutrition in their practices. He ended his address with a plea to the physician to assume leadership in this field.

The conference made a number of specific recom-

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mendations to the President. Briefly, these were the use of the suggested nutritional yardstick (Table 1) as a goal for adequate nutrition; the translation of these allowances into units understandable by the laity; continued nutritional research; the education of all professional groups concerned with nutrition (that is, doctors, dentists, teachers and so forth); the education of the public in nutritional knowledge; the mobilization of any organized unit able to contribute to this campaign; the continued attack on fundamental prob-

formation becomes of more value in the practice of medicine than ever before. An editorial comment in the *Journal of the American Medical Association*<sup>8</sup> concerning this conference is well worth reading.

The highlight of the conference, so far as the practitioner of medicine is concerned, was the promulgation by the Committee on Foods and Nutrition of the National Research Council<sup>9</sup> of recommended daily allowances for the various dietary nutrients (the so-called "yardstick for good

TABLE 1. Recommended Daily Allowances for Specific Nutrients.\*<sup>9</sup>

	ENERGY	PROTEIN	CALCIUM	IRON	VITAMIN A†	THIAMIN (VITAMIN B <sub>1</sub> )‡	RIBOFLAVIN	NICOTINIC ACID	ASCORBIC ACID‡ (VITAMIN C)	VITAMIN D
	cal	gm	gm	mg	int. units	mg.	mg.	mg.	mg	int. units
Man (70 kg)										
Moderately active	3000	70	0.8	12	5000	1.8	2.7	18	75	
Very active	4500					2.3	3.3	23		
Sedentary	2500					1.5	2.2	15		
Woman (56 kg)										
Moderately active	2500	60	0.8	12	5000	1.5	2.2	15	70	
Very active	3000					1.8	2.7	18		
Sedentary	2100					1.2	1.8	12		
Pregnant (latter half)	2500	85	1.5	15	6000	1.8	2.5	18	100	400-500
Lactating	3000	100	2.0	15	8000	2.3	3.0	23	150	400-500
Children up to 12 years										
Under 1 year§	1000 kcal	3-4/kg	1.0	6	1500	0.4	0.6	4	30	400-500
1-3 years	1200	40	1.0	7	2000	0.6	0.9	6	35	
4-6 years	1600	50	1.0	8	2500	0.8	1.2	8	50	
7-9 years	2000	60	1.0	10	3500	1.0	1.5	10	60	
10-12 years	2500	70	1.0	12	4500	1.2	1.8	12	75	
Children over 12 years										
Girls										
13-15 years	2800	80	1.3	15	5000	1.4	2.0	14	80	
16-20 years	2400	75	1.0	15	5000	1.2	1.8	12	60	
Boys										
13-15 years	3200	85	1.4	15	5000	1.6	2.4	16	90	
16-20 years	3800	100	1.4	15	6000	2.0	3.0	20	100	

\*Tentative goal toward which to aim in planning practical dietaries, can be met by a good diet of natural foods. Such a diet will also provide other minerals and vitamins the requirements for which are less well known.

†Requirements may be less if provided as vitamin A, greater if provided chiefly as the provitamin carotene.

‡1 mg thiamin = 333 int. units, 1 mg ascorbic acid = 20 int. units.

§Needs of infants increase from month to month, the amounts given are for approximately 6 to 8 months. The amounts of protein and calcium needed are less if derived from breast milk.

||Allowances are based on needs for the middle year in each group (2, 5, 8 and so forth) and for moderate activity.

¶Vitamin D is undoubtedly necessary for older children and adults, when not available from sunshine, it should be provided probably up to minimum amounts recommended for infants.

Reprinted, with slight modification, with the permission of Dr. Russell M. Wilder, chairman, Committee on Foods and Nutrition, National Research Council. Copies of this chart, with explanatory notes, can be obtained from Nutrition Division, Federal Security Agency, Washington, D. C.

lems of unemployment; the use of any practical device to bring foods to those otherwise unable to afford them, such as the so-called "stamp plan"; the improvement of food distribution; the encouragement of agriculture to a greater production of foods needed in abundance; the encouragement of more production for home use by rural people; and the enrichment of certain staple food products. The realization of these recommendations is certain to have a profound influence for the better on the future health of the Nation and will do much to improve the efficiency of the present defense effort. Nutritional in-

nutrition"); these allowances are given in Table 1. They represent the available scientific knowledge. Nutritional authorities were willing to accept the values tentatively until standards derived from more exact data could be obtained. Foods supplying adequate thiamin, riboflavin and nicotinic acid will tend to supply an adequate amount of the remaining components of the vitamin B group. Diets adequate in protein, calcium and iron will tend to supply other needed minerals, although these are not listed. Adult allowances are given for a man weighing 154 pounds (70 kg.) and for a woman weighing 123 pounds (56 kg.), at the

levels of physical activity, and should be proportionately increased or decreased for larger or smaller persons. Allowances for the vitamin B group are proportional to the caloric intake, and apply to healthy persons, disease may alter them considerably. It is of interest that the protein requirement does not increase with activity in adults. It is increased during pregnancy and lactation, and for children and adolescents. Calcium requirements are discussed in detail elsewhere in this paper. The committee expects nutritional workers to translate these scientific terms into appropriate quantities of foodstuffs available in their own locality and to meet special situations.

The various nutrients provided for in these allowances, with the exception of vitamin D, can be obtained through a diet of natural foods or foods enriched according to the committee's recommendation. Translation of these allowances into a daily dietary pattern of actual foods is given in Table 2. This is an excellent list for the physician

1 demonstrates the nutritional inadequacy of white flour. The superior taste and appearance of white bread originally dictated this change. The nutritional error thus committed did not become apparent until about 1920, and only recently has its full import been appreciated by nutritional experts.<sup>1, 10, 11</sup> In the meantime, several generations

TABLE 3 *Average Values for Whole Wheat White and Enriched Flour*

PRODUCT	CAL CUM	PRO- TEIN PER 100 GMS	IRON	THI- AMINE	RIBO- FLAVIN	NICO- TINIC ACID	VITAMIN D
	mg / lb	mg / lb	mg / lb	mg / lb	mg / lb	mg / lb	USP units
Whole wheat flour	240	1.00	18.0	2.04	1.13	12.3	—
White flour	2	.460	.45	0.23	0.18	3.7	—
Enriched flour*							
Minimum enriched	500†	—	6.0	1.66	1.2	6.0	2.0†
Maximum enriched	2,000†	—	24.0	2.50	1.8	9.0	1,000†

\*Composition of flour enriched according to the definition and standard proposed by the United States Food and Drug Administration.

†Optional ingredients at least for the present.

†This tabulation originally appeared in a report of the Council on Foods and Nutrition, American Medical Association,<sup>12</sup> and is reproduced with the permission of the publisher.

TABLE 2 *Dietary Pattern Suggested by the Committee on Foods and Nutrition, National Research Council<sup>9</sup>*

Food	AMOUNT
Milk	Adults 1 pint children 1/2 pint daily
Egg	Three or four times per week
Meat	One serving (30 gm) at least up to 90 years (for adults)
Vegetables	Two servings (one green or yellow)
Fruit	Two servings (one citrus or banana)
Potato	One or more servings
Ber or fortified oil	100-500 calories
Whole grain or enriched cereal and bread	At least half the intake
Salt and so forth	To complete the caloric requirement

to keep in mind when he attempts to evaluate the adequacy of his patient's diet. It is well to note that half the caloric intake is of whole grain or enriched cereal and bread, and that specific minimums for milk intake are given.

#### NUTRITIONALLY IMPROVED OR ENRICHED FOODS

The introduction of steel roller milling of wheat some seventy years ago cheapened the cost of producing white flour and resulted in its displacement of whole meal flour. Nutritional loss to the public resulted, inasmuch as white flour contains almost no vitamin E and less protein, calcium, phosphorus, iron, vitamin B complex, and carotene than whole meal flour.<sup>10</sup> White flour has been used not only for bread, but for cakes, pies, gravies, sauces, crackers and so forth, and contributes 25 per cent or more to the average daily caloric intake. A comparison of the ingredients of nutritional value of white flour with whole wheat flour is given in Table 3. A further comparison of this table with the requirements listed in Table

have accepted white flour as a major item in their diet and have become accustomed to its use.

Most of the sugar used in this country is refined and hence devoid of minerals and vitamins. The daily per capita consumption of sugar is said to average about 155 gm, which represents 600 calories, or one fourth of all the calories of the diet.<sup>1</sup> Last year, only one fourth of the margarine in the United States was fortified with vitamins.<sup>2</sup> Lard and polished rice, likewise poor vitamin sources, are used extensively.

It is a nutritional fallacy to teach that the balance of the American diet, even if good natural foods are used, will compensate for this 50 per cent or greater caloric content lacking in minerals and vitamins. Reference to Table 2 which lists a truly adequate diet, makes this point clear. Each food is expected to carry its own weight in contributing to the adequacy of the total diet.

The eating habits of the American public are now so well established that a worthwhile change, although not impossible, would be slow. Some favor education of the public to the use of natural foods.<sup>12</sup> The present world crisis makes it imperative that this country secure, as rapidly as possible, the benefits to accrue from application of nutritional knowledge. To this end, fortification or enrichment of foods with nutritional ingredients lost in the manufacturing process is considered a worthwhile solution.<sup>13, 14</sup> Wilder<sup>1</sup> has discussed the inadequacies of solving this problem by urging the public to consume vitamin and mineral pills.

Fortification of food is by no means a new or

untried procedure. Over fifteen years ago, salt was fortified with iodine in the endemic goiter regions, with excellent prophylactic results.<sup>2</sup> Fortification of foods with vitamin D has reduced the incidence of rickets.<sup>2</sup> Fortification of margarine with vitamins A and D was made compulsory in Denmark years ago<sup>1</sup> and has already been used with some of the margarine sold in this country.

The possibilities of enrichments of flour and bread have aroused much interest and comment, as well as some criticism both in this country<sup>1, 7, 11, 13</sup> and in England.<sup>16-18</sup> The Council on Foods and Nutrition of the American Medical Association has recently submitted a detailed report on this subject.<sup>19</sup> There is much to be said in favor of using only natural unrefined foods.<sup>12</sup> However, many objections have arisen to this proposal. In brief, time would be required to change the people's food habits; many do not like the taste or appearance of dark bread; others must avoid the effect of its roughage on their gastrointestinal tract; the baking qualities are not so good as those of white flour; whole-meal flour does not keep so well; and much money is now invested in milling equipment for preparing white flour.<sup>1, 2, 7, 10, 11</sup> One may expect to see the fortification of flour practiced extensively in the future. The British have already fortified their white flour with calcium, iron and thiamin.<sup>16, 18</sup> Fortification of flour is more advantageous than direct fortification of bread, since flour is widely used for other purposes besides bread.

Table 3 gives the average composition of whole-wheat and white flour and, for comparison, the minimum and maximum degrees of enrichment of flour according to the definition and standard proposed by the United States Food and Drug Administration. In principle, this has been endorsed by the Council of Foods and Nutrition of the American Medical Association and by the Committee on Food and Nutrition of the Division of Medical Sciences of the National Research Council. The reason for each figure given is discussed in detail in the council's report.<sup>19</sup> Briefly, the council sponsors "fortification with a limit, that limit being the content of the natural or unprocessed foods." Standards for enriched bread as suggested by the Committee on Food and Nutrition of the National Research Council are given in Table 4. Thus, white bread, with no change in taste or appearance, will approach whole-wheat bread in nutritive qualities. New milling techniques, which preserve more of the original nutritive ingredients of wheat and still produce a white flour, have been perfected, and will be further improved with time. The vitamin B complex of

bread could also be fortified with more nutritious forms of yeast.<sup>19</sup>

Wilder<sup>1</sup> has made several suggestions. If each average daily per-capita portion of sugar (155 gm.) were fortified with slightly more than 30 gm. of skimmed-milk solids, the average American diet would be improved by the addition of the equiva-

TABLE 4. *Suggested Standards for Enriched Bread.*

ENRICHMENT	CALCIUM mg./lb.	PHOSPHORUS mg./lb.	IRON mg./lb.	THIAMIN mg./lb.	RIBOFLAVIN mg./lb.	NICOTINIC ACID mg./lb.
Minimum	300*	—	4.0	1.0	0.8	4.0
Maximum	1200*	—	16.0	2.0	1.6	8.0

\*Optional.

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lent of a pint of skimmed milk. The edible fats, margarine and lard, can be fortified with vitamins A and D. Ascorbic acid is sensitive to oxidation and heating and is therefore less well suited for fortification. However, citrus fruits, tomatoes and potatoes—good to fair food sources of vitamin C—are plentiful in this country. Irradiation of food, to increase its vitamin D content, is already widely practiced. The many suggestions for fortifying foods with calcium are discussed below.

#### NUTRITIONAL ASPECTS OF CALCIUM

In contrast to the many publications dealing with vitamins is the comparatively modest but nevertheless important literature concerned with the nutritional aspects of calcium. With almost no exception, these papers stress the frequent inadequacy of this substance in the American and English diet.<sup>20-23</sup> In fact, the investigative methods of one of the few recent papers<sup>24</sup> to contradict this point of view were immediately criticized, and its results discounted.<sup>25-27</sup> Although realizing the significance of an adequate calcium intake for infants and young children, few physicians have paid much attention to the calcium intake of adults. The metabolism of calcium, phosphorus and vitamin D is closely related and interdependent. Phosphorus is present in many foods, so that diets are rarely deficient in this substance. Foods adequate in protein contain sufficient phosphorus. In fact, no specific mention of phosphorus requirements was given at the National Nutrition Conference (Table 1). Practically none of the common foods are adequate in vitamin D. Infants and children now almost universally receive fish-liver oil, viosterol or irradiated foods to supply this deficient vitamin. And its use during pregnancy and lactation is rapidly increasing. Adults

with no opportunity for exposure to sun may require supplementation of their diet with vitamin D (Table 1).

Of the aforementioned triad, calcium is the substance that is likeliest to be deficient in the average diet; rarely is an attempt made to remedy this fault.

Of the total calcium content of the body, 99 per cent is contained in the bones, none in the red blood cells, a small amount in tissue fluids and 9.5 to 11.5 mg. in each 100 cc. of blood serum.<sup>28, 29</sup> The necessity of the blood calcium for normal neuromuscular irritability, clotting of blood and so forth is too well known to require comment.

Active adults with normal endocrine and renal function, an adequate supply of vitamin D and proper intestinal absorption maintain a normal blood-calcium level regardless of the adequacy of the dietary calcium; calcium is removed from the trabeculae of the bones when the calcium balance is negative and stored when the supply is great.<sup>28</sup> Urinary and stool excretion of calcium continues, even when the dietary intake of calcium is low or absent. The influence on bone metabolism of long-continued dietary calcium deficiency, with resultant negative calcium balance, has aroused much interest in recent years.<sup>30-34</sup> Vitamin D and a sufficient amount of phosphorus are essential for the proper metabolism of calcium, as is normal parathyroid function. The presence of hydrochloric acid, sucrose, lactic acid and citric acid in the gastrointestinal tract favors calcium absorption.<sup>22, 35</sup> Alkalies, excess fats, excess phosphates, oxalic acid (present in leafy vegetables), maltose and starch interfere with its absorption.<sup>22</sup> The phytic acid of cereals was formerly believed to immobilize calcium.<sup>35</sup> However, in more recent studies, calcium phytate proved to be readily absorbed.<sup>36</sup> By interfering with the utilization of vitamin D, the ingestion of mineral oil in growing dogs has been found to result in poor retention of both calcium and phosphorus, with the development of rickets.<sup>37</sup> This may or may not be of clinical significance. The ration used contained 5 to 10 per cent mineral oil, proportionally more than is likely to be used by human beings. All this emphasizes the complexity of the problem of calcium absorption and the need for a safe margin over the amount estimated for maintenance requirements. At best, only 20 to 30 per cent of calcium ingested by adults and older children is utilized.<sup>33</sup>

Milk and cheese are the only good sources of calcium in the diet, and in their absence it is exceedingly difficult to fill the calcium need through

food alone.<sup>22</sup> The inadequacy of calcium in other foods is well illustrated in a table prepared by Bernheim.<sup>22</sup> To secure 0.70 gm. of calcium daily from any other single food, it would be necessary to eat 3.2 lb. of beans, 7.3 lb. of white bread, 5.5 lb. of brown bread, 11.0 lb. of butter, 1.5 lb. of cauliflower, 27.5 lb. of corn, 20 eggs, 2.3 lb. of oatmeal, 17.0 lb. of potatoes, 4.9 lb. of oranges, 26.4 lb. of lean meat, 14.7 lb. of fish and so forth. Furthermore, the oxalic acid present in some leafy vegetables prevents adequate absorption by the formation of insoluble calcium oxalate in the intestinal tract.

A quart of milk contains slightly more than a gram of calcium (1.16 gm.)—a useful figure to commit to memory. An economical source of milk looms large as a factor in arranging for an adequate supply of calcium in diets of persons in the low-income group.<sup>38</sup> Koehn<sup>39</sup> has some interesting recommendations in this regard. A 1¼-in. (3.2-cm.) cube (30 gm.) of yellow cheese may be substituted for half a pint of milk. This contains about 0.25 gm. of calcium. Skimmed milk or butter-milk is the equivalent of whole milk in calcium and protein, but not, of course, in fat or the fat-soluble vitamins, and is much cheaper.<sup>39</sup> Both are excellent sources of calcium for persons attempting to lose weight. Evaporated milk is the equivalent of whole milk in calcium content and is less expensive. Dry skimmed milk (dry milk solids) has the food value of whole milk, except for the fat, and is cheaper. One quarter of a pound (120 gm.) of dry skimmed milk, diluted with water, makes a quart of fluid skimmed milk. Milk used in cooking, desserts made from milk, ice cream, because of milk content, and so forth, add to the calcium content of the diet. For all practical purposes, a check on the calcium content of a patient's diet concerns information on the use of these items.

From the evidence already presented, the frequency of calcium deficiency in the American diet becomes understandable. Serious consideration has been given to various plans to increase the calcium content of staple foods. The supplementation of white flour with calcium, to a maximum of 2000 mg. per pound (Table 3), is one proposal. The addition of milk solids to cane sugar is another.<sup>1</sup> The British have already added 7 ounces (210 gm.) calcium carbonate (*creta praeparata B.P.*) to each 280-pound sack of white flour used in the preparation of their so-called "war loaf." Fortification of breakfast cereals with calcium is another suggestion. For example, Pierce and others<sup>40</sup> found that when part of the milk calcium of an adequate diet fed to children was re-

placed by an equivalent amount supplied by tricalcium phosphate in a fortified cereal, utilization as measured by retention was equally good from milk and cereal.

Furthermore, direct supplementation of the diet with one of the calcium salts is entirely possible if an adequate supply of food calcium is lacking. A number of studies indicate that this substitution is practical on an extensive scale. Aykroyd and Krishnan<sup>41</sup> during a four-month period gave children (ages two and a half to seven) in a nursery school in South India 0.5 gm. of calcium lactate daily. The children showed greater increases in weight, height and general well-being than a control group of children in the same school who did not receive the supplement. These authors recommend that calcium salts be used as a partial substitute for milk when the latter cannot be obtained. Gaunt and his associates<sup>42</sup> had previously shown that improvement exhibited by a large colony of rats (reared for generations on an average diet eaten by a working-class community in Scotland) when greens and milk were added to this diet could be duplicated in large part by adding mineral supplements of calcium and phosphorus. In human practice, increased consumption of milk was recommended as the best means of improving the diet whenever it was possible.

Gunderson<sup>43</sup> discusses the economics of the use of calcium salts. Precipitated calcium carbonate is listed as the most economical source, calcium gluconate as the most expensive. Calcium triphosphate, calcium phosphate (bone meal), calcium diphosphate, calcium monophosphate, calcium citrate and calcium lactate range between these in this order.

The calcium requirements for human beings have been worked out by means of calcium and phosphorus studies, the presence and degree of positive or of negative calcium balance for various levels of calcium intake being determined. In addition, the rate of growth and weight of the skeletal structure has been considered. Leitch<sup>44</sup> reviewed the literature dealing with this subject. By such means, the minimal or maintenance requirement for calcium is determined. Optimal requirements used for clinical purposes are determined by adding 50 per cent to this minimal level to allow for possible difficulties in utilization (as was noted above in the discussion on the absorption of calcium).

For many years, Sherman's<sup>23</sup> estimate of 0.45 gm. of calcium as the minimal and 0.70 gm. as the optimal daily requirement for an adult weighing 154 pounds (70 kg.) was the accepted standard. Owen<sup>45</sup> found 0.52 gm. to be the minimum,

whereas Leitch,<sup>44</sup> from an extensive survey, gave 0.55 gm. as a minimum. The optimal daily allowance for calcium as recommended by the Committee on Foods and Nutrition of the National Research Council is given in Table 1: 0.8 gm. for adult men and women, 1.5 gm. during pregnancy, 2.0 gm. during lactation, 1.0 gm. for small children, and 1.3 to 1.4 gm. from puberty until growth is completed.

The greater need for calcium during the years of growth, pregnancy and lactation should be constantly kept in mind. The difficulty of sustaining lactating women in a positive calcium balance has been emphasized.<sup>46</sup> The calcium problem in obstetrics has been discussed by Bear<sup>47</sup> and by Mendenhall and Drake.<sup>48</sup> The diet during puberty needs special attention. In a survey in Toronto among families able to supply a reasonably good diet, the lowest intake of calcium and milk was found in the girls in their teens, explainable on the current desire of girls to be slim.<sup>49</sup> McHenry urges that this group be educated to realize that an adequate knowledge of nutrition allows one to avoid obesity and still to be properly fed. Skimmed milk or dry milk solids may be substituted for whole milk if the fear of obesity causes the latter to be omitted from the diet.

What ill effects are to be expected when adults live for years on a diet deficient in calcium? Many recent papers<sup>30, 32, 34, 44</sup> have attempted to correlate the considerable incidence of osteoporosis among persons past middle life with this factor. Nervous irritabilities have likewise been attributed to this cause.<sup>30</sup> However, the cause of senile osteoporosis is by no means settled. Among the possible explanations are: long-continued dietary calcium deficiency, with negative calcium balance and gradual demineralization of the skeleton<sup>31</sup>; deficiency of vitamin D<sup>33</sup>; inability to absorb mineral salts from the gastrointestinal tract with advancing years<sup>33</sup>; the presence of achlorhydria in old age<sup>32</sup>; atrophy of bone due to disuse as the result of restricted physical activity in old age<sup>50</sup>; and senescent changes.<sup>50</sup>

Albright and his co-workers<sup>50</sup> have described postmenopausal osteoporosis, a form of bone disease often confused with senile osteoporosis, and attribute it to the endocrine changes following the menopause. A beneficial effect of estrogen therapy on the retention of calcium in this condition was noted. They consider osteoporosis a disease in which the osteoblasts are primarily deficient in laying down osteoid tissue, and believe that a negative nitrogen balance may interfere with osteoblastic activity in laying down the necessary organic matrix. Such a factor could well be present



in old age. Adequacy of protein in the diet thus becomes a factor to be considered in the etiology of senile osteoporosis.

Owen, Irving and Lyall<sup>34</sup> made calcium balance studies of 7 male patients over seventy years of age; 4 of them manifested osteoporosis by roentgenographic examination. Three were in calcium equilibrium with intakes of only 0.3 gm calcium. The authors believe that their results suggest adaptation by the body to the continued smaller calcium intake by a lower rate of calcium turnover and a lessened reserve of calcium in the skeletal stores; they conclude that prolonged nutritional calcium deficiency may result in generalized osteoporosis in elderly patients. Leitch<sup>44</sup> subscribes, in part at least, to the theory that senile osteoporosis is due to prolonged calcium deficiency. The study of Adams, Boothby and Snell<sup>51</sup> indicates that treatment of senescent osteoporosis with calcium salts can convert a negative calcium balance to a positive one and thus store calcium and phosphorus. Their subject, a sixty-five-year old woman with osteoporosis, stored over a nineteen week period 29.3 gm. of calcium and 13.3 gm of phosphorus, a ratio of 2.2:1—or the ratio of these substances in bone.

These studies seem to indicate that adequate calcium, protein and vitamin D nutrition throughout life may prevent the development of osteoporosis in old age. Furthermore, treatment of senile osteoporosis with a diet adequate in protein and calcium, supplemented with calcium and phosphorus salts and vitamin D, has some rationale as a therapeutic procedure. To be successful, it will probably have to be continued for a long time.

The nature and the amount of the dietary intake of calcium, aside from its purely nutritional aspects, are often of diagnostic or therapeutic interest in the practice of medicine. For example, in using the Sulkowitch reagent to test for calcium in the urine, one should remember that normal persons may show excess urinary calcium shortly after drinking a large amount of milk.<sup>29</sup> This may be confused with hypercalciuria due to disease. Albright,<sup>29</sup> in discussing the treatment of hypoparathyroidism, stresses the need for a high intake of calcium and a low intake of phosphorus, but adds that, in spite of its high calcium content, milk is contraindicated because it is likewise high in phosphorus. Persons with prolonged recumbency and immobilization of the body because of injury or disease often have hypercalciuria due to demineralization of the skeleton, with the formation of renal calculi. Carlson and Ockerblad<sup>52</sup> point out that the use of much milk, the basis of most sickroom diets, often leads to excessively high calcium intakes, which become an additional

factor to be considered under such circumstances in explaining the calculus diathesis. Barney and Jones<sup>53</sup> suggest that ingestion of excessive amounts of milk and cheese, especially when the urine is alkaline, may, by precipitating calcium phosphate in the urine, be a factor in the formation of calculi in the urinary tract. Kempster and others<sup>54</sup> recommend that persons allergic to milk secure their daily calcium requirement as dicalcium phosphate, with a percentage utilization equal to the calcium in milk. Albright<sup>29</sup> has emphasized the fact that the characteristic bone changes of hyperparathyroidism may be lacking if the patient's diet has contained sufficient calcium to balance the excess urinary calcium loss. Such persons are invariably heavy milk drinkers. Diagnosis then rests on the chemical findings in the blood, the presence of renal calculi, systemic symptoms and so forth.

### NUTRITION IN OLD AGE

Many publications have appeared in recent years stressing the importance of the study of disease in old age. In fact, the rise of the specialty of geriatrics—the old-age counterpart of pediatrics—is foreseen,<sup>55</sup> a possibility by no means unlikely in view of the increasing proportion of older people in this country's population. Official cognizance of the senescent individual in the national life and economy was recently taken by the United States Public Health Service with the establishment of a Unit of Gerontology at the National Institute of Health.<sup>56</sup> Under the editorship of Cowdry,<sup>57</sup> the known facts concerning the aging process have been reviewed.

Sherman<sup>58</sup> believes that the nutritional knowledge already available will, if properly applied, “add life to our years,” and “. . . add years to our lives.” Food and nutrition have now been accorded a place, along with heredity, in the control of longevity. The praiseworthy results of the increasing appliance of the nutritional principles in the practice of pediatrics are too well known to need any comment. One already finds cautious suggestions<sup>1, 2, 3, 59</sup> that long continued inadequacy of diet may be a factor in the early development of degenerative diseases. Naturally, to be truly effective, such dietary principles must be applied early in life. Harris<sup>60</sup> aptly emphasizes the fact that the effective practice of geriatrics must begin where the pediatrician leaves off. The effects of a lifetime of unhygienic habits and an incorrect diet cannot be righted, once old age is reached. The practitioner of medicine—the family doctor—is thus entrusted with the promulgation of this thesis. An inquiry into a per-

son's habits of eating and recommended dietary changes, as the circumstances require, may well become a routine part of the annual health check-up now being widely recommended to the public by many agencies.

Diminution of appetite is common in old age, and its causes and remedies have been discussed by Meyer.<sup>61</sup> This, coupled with the fact that many elderly people because of loss of teeth and inadequate artificial dentures are unable to chew properly, frequently marks the onset of a poor dietary regime in old age. The latter cause is commonly responsible for the clinically detectable deficiencies noted in old people studied on the medical wards of the Boston City Hospital.<sup>62</sup> Meyer and his co-workers<sup>63</sup> found that old people have less salivary secretion of ptyalin than young adults, with resultant deficiency of starch digestion in the mouth and stomach. Whereas 50 gm. of white bread is easily digested in the mouth and stomach of young people, only 0.5 gm. is digested by old people.<sup>63</sup> Masticatory difficulties in old age often necessitate a soft diet, relatively high in carbohydrates and low in protein. However, the same workers<sup>64, 65</sup> found in a later study that the total intestinal digestion of carbohydrates was not markedly disturbed, because the pancreatic amylase, although slightly subnormal, was sufficient to complete this digestive process. They occasionally noted, in fact, abnormally high values for this pancreatic enzyme in the age group from eighty-one to one hundred years. These levels were considered to be possibly compensatory for the lowered salivary ptyalin of old age. Both proteolytic enzymes (pepsin and trypsin) were found to be diminished in old age, but they concluded that the concentration was adequate to meet the requirements of the usually decreased protein intake. They admit, however, that some old people consume large quantities of protein, with apparently normal digestion. They conclude their paper by stressing the fact that such studies may be helpful in rationalizing the dietary management of old persons.

The incidence of achlorhydria is known to increase with advancing age.<sup>66</sup> The influence of achlorhydria on the absorption of various substances in the diet and their utilization by the body may be important. Its interference with the absorption of iron has been established. Less is known of its influence on the absorption of fractions of the vitamin B complex and other dietary factors. Leitch<sup>44</sup> comments on the need for more knowledge of its relation to the absorption of calcium, a subject worthy of investigation, in view of the frequency of osteoporosis in old age.

Interference with eating in old age commonly results from digestive symptoms. Meyer<sup>61</sup> stresses their frequency, and emphasizes that cardiac, renal and hematologic disorders, all particularly common at this time of life, may be factors in producing such symptoms, apart from diseases primary in the gastrointestinal tract. Physiologic changes incident to the aging process are undoubtedly additional factors in causing such symptoms. All this serves to emphasize again that maintenance of adequate nutrition is often more difficult in old age than in early life.

Tuohy<sup>67</sup> found that undernutrition in the aged was more frequently the result of perverseness of appetite than economic adversity. He noted that old people often limit their diet because of faulty advice or inherent fear of eating adequately. The *Journal of the American Medical Association*<sup>68</sup> has commented editorially on this subject.

Owen<sup>15</sup> and Robertson,<sup>69</sup> from calcium balance studies on old men, found their requirements to be much the same as those of young adults, with a further similarity that they readily retained calcium and phosphorus after depletion. Increasing age did not offset long subjection to a diet low in calcium.

The significance of long-continued negative calcium balance on the genesis of senile osteoporosis has already been discussed.

The average 10 per cent reduction in the basal metabolic rate of old age<sup>70</sup> and the lowered physical activity indicate the need for reduction in caloric intake. The adverse influence of obesity on longevity is well recognized. The diet of old age must therefore be planned to avoid this factor and eliminate it if it is already present.

Vitamin deficiencies, especially of minor degree or with atypical manifestations, are common in old age.<sup>67</sup> Tuohy<sup>67</sup> remarks that gastrointestinal atony may respond to the use of thiamin. Mental changes often ascribed to the aging process may be due to nicotinic acid deficiency.<sup>71</sup>

Piersol and Bortz<sup>72</sup> suggest the use of liver twice weekly, in addition to iron-rich foods, to maintain the red-cell count at a normal level; milk is urged as an ideal food for old age. They also comment that a minimum fat content is in order. Horn<sup>73</sup> likewise considers fats to be the least of the dietary essentials of old age. Tuohy<sup>74, 75</sup> extols the high-protein diet in old age as protective against inadequate hematopoiesis and, indirectly, liver insufficiency. He also urges a freer diet and less fear of food with old people.<sup>67</sup> Barovsky<sup>76</sup> reports that milk fortified with minerals and vitamins was well tolerated by a group of 30 senile persons. Tuohy<sup>67</sup> reports that arteriosclerotic persons often

tolerate several light meals better than a smaller number of heavy ones

One may conclude from these papers that persons in the old age group can often support an adequate diet. Such a diet should be of low caloric content, with a minimum of fat, and adequate in protein, it should contain liver and iron rich foods and, above all, milk. The last may be given as skimmed milk if the fat content is to be avoided. Adequate intake, if necessary by supplementation, of all the vitamins is much to be desired. Since old people have but little exposure to sun, the addition of vitamin D should not be overlooked. Smaller and more frequent meals are often required. If the teeth are absent special care is needed to prevent inadequacies of the diet. Under such circumstances, milk becomes of even greater benefit as a primary food. Osteoporosis of old age may be preventable under such a regime.

#### MISCELLANY

Bourne's book, *Nutrition and the War*, an English publication, is typical of several that attempt to educate the public in the essentials of nutrition and thus to prepare them to make the most nutritionally of every food, should the supply and variety be curtailed by war conditions. Familiarity with such material will enable physicians to give dietary advice in terms that the average layman can appreciate and understand. American physicians are not faced with the practical realities of this problem as their British colleagues are. The papers by Booher<sup>8</sup> and Koehn<sup>9</sup> give some excellent practical advice on the economic aspects of diets as related to conditions in this country.

Orr<sup>7</sup> discusses a hypothetical wartime diet for the general population of England that illustrates the possibility of making a satisfactory diet from a small number of foods, many of which could be produced in England. Of interest is the fact that this limited diet would be more adequate than the prewar diet of the poorest 10 per cent of the population. The study points out that all the nutrients required by the body can be obtained from a few foodstuffs. This wartime diet consists of a daily ration of 0.6 pint (300 cc) of milk, 6 ounces (180 gm) of vegetables, 16 ounces (480 gm) of potatoes and 2 ounces (60 gm) of oatmeal,—is protective foods,—and 11.8 ounces (350 gm) of bread, 1.8 ounces (55 gm) of fats and 1 ounce (30 gm) of sugar—as energy yielding foods. An important objective of such a diet is to supply protective foods first, then as many energy yielding foods as are required to complete the desired caloric intake. Restrictions, if necessary, should apply to the latter first. Heavy work and army duty

would, of course, require the above diet to be increased.

Drazin<sup>80</sup> reviews representative examples of diets from various parts of the world to illustrate that monotony in diet is not detrimental to good health provided it is adequate from a nutritional viewpoint. As advantages for such a diet, he lists inexpensiveness, less trouble in preparation and less conduciveness to overeating, with resultant obesity and other metabolic disorders. Such statements are reassuring in the event that the variety of foods should be curtailed because of war conditions.

Except for iodine, which is required for proper thyroid function, and possibly copper, the significance of the so called 'trace elements' in the diet is not well established. Evidence indicates that they may be indispensable constituents of intracellular enzyme systems. Underwood,<sup>81</sup> Shohl<sup>82</sup> and Daniel<sup>83</sup> recently reviewed this subject and have listed detailed bibliographies. No direct clinical application to nutrition is in order at this time.

The influence of heating,<sup>11, 84</sup> canning,<sup>11</sup> and quick freezing<sup>85</sup> on the nutritive value of foods has continued to receive attention. It is of interest that the values recommended by the National Research Council (Table 1) refer to the amount of each factor actually eaten and make no allowance for extensive losses in cooking.<sup>9</sup>

The soybean is a new addition to the dietary of this country and is gaining rapidly in popularity.<sup>86, 86</sup> It is an unexcelled substitute for meat, its 36.5 per cent protein being of a variety closely resembling animal protein. It also contains about 20 per cent fat and 20 per cent carbohydrates.<sup>80, 86</sup> Soybean flour in any proportion up to 30 per cent can be used with white or whole wheat flour.<sup>81</sup> The Germans are reported to be using it extensively in various forms—the so called 'Nazi food pills'—as in army ration.<sup>87</sup>

Bourne<sup>88</sup> discusses the 'satiety value' of foods and points out that it is no indication of their nutritional value. Hunger is rapidly satisfied by sugar, butter, fatty foods, milk, potatoes, meat and eggs, but poorly satisfied by bread, green vegetables and nonfatty fish. As is well known, satisfaction of 'hollow hunger' is no guarantee of good nutrition. It must, however, not be neglected in planning any dietary regime. Hungry people are neither content nor efficient.

Johl and Cluver,<sup>89</sup> in a comparative study of the growth of physical efficiency of children from poor homes as contrasted with those from economically better situated homes, found no difference in the prepubertal age group but a striking difference in

favor of the latter after puberty. They concluded that, in the absence of true clinical deficiency, undernutrition of lesser degrees did not impair the growth of physical efficiency in the early years of life. However, the additional strain occasioned by bodily changes at the time of puberty caused a distinct lessening of the growth of physical efficiency unless the quality of the diet was improved. Table 1 shows the increased nutritional requirement at puberty suggested by the Committee on Foods and Nutrition of the National Research Council. Physicians responsible for the care of children should impress parents with the necessity of this dietary change at the time of puberty.

Many physicians find it difficult to avoid loss or interruption of sleep, long hours of work, nervous tension and improper care of their own minor ailments. However, adequate nutrition is within the grasp of each one. Olmsted<sup>90</sup> has written an interesting paper concerning the diet of the doctor. He believes that physicians who have good nutritional habits are sound advisers to their patients on this matter, and it affords them at least one opportunity to practice what they preach.

Sinclair<sup>91</sup> has reviewed the nutritional significance of fat in the diet. Reduction of fat in the diet when the caloric value is obtained mostly from crude high-carbohydrate foods—a situation common in Europe today—results in premature hunger and a reduced capacity to do sustained work. Wilder<sup>92</sup> also discusses the reality of "fat hunger." The per-capita consumption of fat in the occupied European countries is now less than 30 gm.,—less than one quarter of the prewar level,—for the German people 60 gm. and for the German soldier 90 gm. The fat supply is ample in this country.

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favor of the latter after puberty. They concluded that, in the absence of true clinical deficiency, undernutrition of lesser degrees did not impair the growth of physical efficiency in the early years of life. However, the additional strain occasioned by bodily changes at the time of puberty caused a distinct lessening of the growth of physical efficiency unless the quality of the diet was improved. Table 1 shows the increased nutritional requirement at puberty suggested by the Committee on Foods and Nutrition of the National Research Council. Physicians responsible for the care of children should impress parents with the necessity of this dietary change at the time of puberty.

Many physicians find it difficult to avoid loss or interruption of sleep, long hours of work, nervous tension and improper care of their own minor ailments. However, adequate nutrition is within the grasp of each one. Olmsted<sup>90</sup> has written an interesting paper concerning the diet of the doctor. He believes that physicians who have good nutritional habits are sound advisers to their patients on this matter, and it affords them at least one opportunity to practice what they preach.

Sinclair<sup>91</sup> has reviewed the nutritional significance of fat in the diet. Reduction of fat in the diet when the caloric value is obtained mostly from crude high-carbohydrate foods—a situation common in Europe today—results in premature hunger and a reduced capacity to do sustained work. Wilder<sup>92</sup> also discusses the reality of "fat hunger." The per-capita consumption of fat in the occupied European countries is now less than 30 gm.,—less than one quarter of the prewar level,—for the German people 60 gm. and for the German soldier 90 gm. The fat supply is ample in this country.

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DR. TRACY B. MALLORY: He had it nine years before entry and again on entry; that is the extent of our information.

DR. BAUER: Do you know anything about the initial illness? Did he have fever or jaundice, and why was he kept in the hospital so long?

DR. MALLORY: I cannot answer the questions.

DR. BAUER: The rash resembling hives is of no diagnostic help to me. Did this man ever have any symptoms suggesting duodenal ulcer?

DR. MALLORY: I do not know.

DR. LOWREY F. DAVENPORT: The best story came from the outside doctor, who followed the case for fifteen years and was convinced that the bleeding nine years before entry was quite typical of ulcer; x-ray examination in several places confirmed the diagnosis. The patient had had a protuberant abdomen for years, and because of this we had a great deal of difficulty persuading him to come to the hospital. He said that his abdomen had always been large, and not until we showed him that his trousers lacked 10 inches of meeting was he convinced that he was unusually large.

DR. BAUER: He had a swollen abdomen. We do not know how much significance to attach to the abdominal findings, because determining the size of the liver and spleen under these conditions is always difficult.

Patients with cirrhosis may require innumerable paracenteses over a period of years. It is possible to have ascites due to portal obstruction for a period of nine years. On the other hand, unless the history is very inadequate, the patient was extremely well between the episodes of gastrointestinal bleeding; I should therefore be inclined to believe that there were times when he had little or no ascites.

The chest signs, I presume, were consequent to the large amount of ascitic fluid.

The temperature of 104°F. is probably of significance, particularly in that we are dealing with a man who had what would seem best interpreted as portal obstruction. He obviously had suffered from gastrointestinal bleeding from time to time, and this was the reason for his seeking hospital admission. That he was jaundiced is shown by the van den Bergh reaction.

The ascitic fluid, from the information given, seems to have been a transudate rather than an exudate. Was it by any chance injected into a guinea pig?

DR. MALLORY: No.

DR. BAUER: A roentgenogram subsequent to the injection of Thorotrast showed very little increase in density of the liver. This finding would be in keeping with the diagnosis of chronic liver

disease, such as cirrhosis, because Thorotrast is taken up by the reticuloendothelial system. If the liver is diseased, one expects a reduction in that system and, consequently, no increase in density of the liver, following the injection of this substance.

Have we the x-ray films here? Is there any suggestion of pulmonary disease? Is there any reason to believe that the patient had tuberculosis?

DR. JAMES R. LINGLEY: The lungs are clear, except for this atelectasis at the base, as described. The diaphragm is high on both sides, probably because of ascites, and this leads to some compression atelectasis at the bases, more marked on the right. The lungs are otherwise clear. The aorta is quite tortuous. This is the area referred to in the inferior margin of the glenoid fossa, about which I cannot help you very much. The changes are very indefinite. The first thing I should think of is Paget's disease, but it could be metastasis.

DR. BAUER: Is there any reason to suspect tuberculosis?

DR. LINGLEY: No; this is the abdominal film, showing the spleen enlarged and increased in density by Thorotrast. The liver, on the other hand, is much less dense than the spleen. It should be denser after Thorotrast. It does not appear to be enlarged.

DR. BAUER: You do not think this could be an end result of septic arthritis some years previously?

DR. LINGLEY: The changes are too localized, and there is no narrowing of the joint spaces.

DR. BAUER: Do you think that the bone is denser here than here?

DR. LINGLEY: It looks a little irregular and increased in density along the margin. I should put Paget's disease first.

DR. BAUER: I should think there was little doubt that we are dealing with a man who had physical findings consistent with portal obstruction due to cirrhosis of the liver. In addition, he had a suppurative, cervical adenitis. The very fact that the latter had been present on two occasions previously and had been incised some eight weeks before and was still draining leads me to believe that this man had, in addition to a portal obstruction, tuberculous adenitis. We have from the history good reason to think that he had evidence of portal obstruction in the initial illness nine years previously. I further believe that he had sufficient improvement in liver function to be able to carry on fairly normally for some time thereafter. The fact that he did not use alcohol

was in his favor, and may have been responsible for his having lived so long. There are a number of questions to which we should like to know the answers. What was the cause of the repeated hematemesis? The patient had been x-rayed on three occasions in two or three different institutions, and each time he was reported to have a duodenal ulcer. On the other hand, according to my interpretation, he was suffering from a disease that is sometimes complicated by hematemesis, namely, portal cirrhosis of the liver. He had three massive hemorrhages and lived nine years. If the bleeding was from esophageal varices, it is very unusual, but I suppose it could and I believe it does happen; therefore, bleeding alone does not enable us to state whether these hematemeses always resulted from a duodenal ulcer or varices or perhaps both. I am a little inclined to believe, although I am unable to prove it, that the final hematemesis could very well have been due to bleeding from esophageal varices. If we are dealing with a man who had evidence of portal obstruction due to cirrhosis for at least nine years, esophageal varices would not be unusual. I take it that no gastrointestinal examinations were made here.

DR. MALLORY: None were made in this hospital.

DR. BAUER: If varices were looked for, they were not found, or at least they were not mentioned in any of the x-ray reports. I rather hesitate to throw out the diagnosis of duodenal ulcer.

What was the cause of the fever? A suppurative adenitis is sufficient cause for a temperature of 104°F. However, patients with cirrhosis may run a low-grade fever. The combination of the suppurative adenitis and cirrhosis of the liver would adequately account for the fever. The intercurrent infection probably served as a sufficient additional load on the liver to precipitate serious liver failure. One might explain the fever on the basis of such a combination of factors. The very fact that this man had cirrhosis for at least nine years means that we must bear in mind the possibility of a hepatoma, which may also cause fever.

There remains still another possibility, namely, tuberculous peritonitis, a complication of cirrhosis of the liver. I have interpreted the cervical adenopathy as being tuberculous in nature and therefore wonder if a hematogenous spread had not resulted in tuberculous peritonitis. If this occurred, we must also raise the possibility of miliary tuberculosis. The cause of death was obviously hematemesis in a man who was seriously ill at the time he entered the hospital. As I said be-

fore, I believe that the final hematemesis was due to bleeding from esophageal varices.

We might reconstruct this story as follows: catarrhal jaundice twenty-five years previously, followed by cirrhosis of the liver, an occasional sequela. Subsequently, an exacerbation of the tuberculous adenitis, with eventual dissemination of tubercle bacilli, resulted in tuberculous peritonitis and perhaps tuberculosis elsewhere. This added infection was responsible for further injury to the liver. The last hematemesis was responsible for his exitus. I realize that a diagnosis of tuberculous adenitis and cirrhosis of the liver, in addition to hemorrhage from either a duodenal ulcer or an esophageal varix, is adequate to account for all that this man showed, but I am rather intrigued with this other possibility, because we know that tuberculous peritonitis is one of the complications of cirrhosis of the liver.

For my final diagnosis, I shall say that this man at autopsy showed cirrhosis of the liver, tuberculous adenitis, tuberculous peritonitis, healed duodenal ulcer, possibly miliary tuberculosis and possibly hepatoma, and that he died of ruptured esophageal varices. The x-ray changes in the glenoid fossa are left unaccounted for. If my memory serves me correctly, metastases from hepatoma are not very common, especially this far removed.

DR. MALLORY: Hepatoma does metastasize to bone.

DR. BAUER: Yes; but it is not very common. This picture is consistent with Paget's disease, and I should like to account for the bone lesions on this basis. This would make my interpretation much easier.

DR. J. H. MEANS: I should like to cite a case with several points of similarity that bear on the combination of cirrhosis of the liver and hematemesis. Several years ago, there was a man, older than this one, who the service thought had the classic picture of cirrhosis of the liver, with ascites, hematemesis and so forth. We thought, of course, that he was bleeding from varices but the X-ray Department persistently refused or were unable to find any varices, which was a little disconcerting. The patient died, and it was proved that he did not have cirrhosis of the liver or varices and bled from a duodenal ulcer.

DR. BAUER: I do not see how one can say that this mistake did not occur in this case. I realize that it is rather foolish of me to assume that the hemorrhage came from esophageal varices. After all, three hospitals have stated that he had a duodenal ulcer, and it is hard to go against these reports. On the other hand, a man who has had



cirrhosis of the liver for nine years is an excellent candidate for esophageal varices

DR. WILLIAM RICHARDSON. What about the specific gravity of the abdominal fluid? It was 1.010. Would that be evidence against tuberculous peritonitis?

DR. BAUER: I think it would. On the other hand, marked ascites and slight exudation might give such a figure. That would not disturb me unduly.

DR. MALLORY. A point raised by Dr. Chester M. Jones was that the patient had just had a large hematemesis. Ascites frequently occurs after hemorrhage as the result of a sudden lowering of the serum protein. Such a mechanism might affect the specific gravity of the fluid

#### CLINICAL DIAGNOSES

Abscesses of liver, multiple.  
Cirrhosis of liver, toxic

#### DR. BAUER'S DIAGNOSES

Cirrhosis of liver  
Tuberculous adenitis  
Tuberculous peritonitis  
Duodenal ulcer, healed.  
Miliary tuberculosis?  
Hepatoma?  
Ruptured esophageal varices

#### ANATOMICAL DIAGNOSES

Liver abscesses, multiple.  
Tuberculous cervical adenitis and peritonitis  
Miliary tuberculosis, generalized  
Cholecystitis, chronic.  
Cholelithiasis.  
Choledocholithiasis  
Esophageal varices (no thrombosis of portal and splenic veins)  
Ascites

#### PATHOLOGICAL DISCUSSION

DR. MALLORY. Several of Dr. Bauer's predictions are correct, but the bases on which he founded his reasoning are almost entirely incorrect as judged from the results of autopsy. The patient had a generalized tuberculosis, with frankly caseous cervical lymph nodes, with an extremely extensive tuberculous peritonitis and with miliary tubercles throughout the spleen and liver. There was no cirrhosis. There was no mechanical portal obstruction. I did not believe the intern, and I personally dissected out the portal vein. There were esophageal varices, unexplained, and no trace of any ulcer in the duodenum or any scars. There were two very large liver abscesses, one 3 and

one 5 cm. in diameter. There were stones in the gall bladder and the common duct, and there was a cholangitis. I believe that the liver abscesses were pyogenic in character. On smear, the pus contained many diphtheroid bacilli; no tubercle bacilli were found. The explanation for the varices in the absence of portal obstruction, I cannot offer. I have seen it four or five times, and it does occur.

One can only guess, it seems to me, in retrospect about the ascites nine years before entry. Tuberculous peritonitis at that time with spontaneous recovery is the best guess. One certainly does see spontaneous recovery from tuberculous peritonitis, and I cannot believe that he could have had a portal obstruction that left no trace.

DR. WILLIAM B. BREED. What was the size of the liver and spleen?

DR. MALLORY. The spleen weighed 600 gm.; the liver was normal in size, weighing 1500 gm.

A PHYSICIAN: What were the other cases of varices and no portal obstruction?

DR. MALLORY. They occurred chiefly in elderly men. I remember only one specifically, a man in the late seventies or early eighties, with massive hematemesis from esophageal varices but no portal obstruction.

DR. BAUER. Do you conclude that he did not have duodenal ulcer and that he had always bled from varices?

DR. MALLORY. It is the only conclusion I can reach.

DR. RICHARD H. SWEET. What did the clinicians have in mind when they gave Thorotrast—liver abscess?

DR. MALLORY. It sounds as if they did.

DR. DAVENPORT. It was given at the suggestion of Dr. Jones, who believed that the prognosis was hopeless, and that there was no danger in giving it. He hoped to outline an abscess or hepatoma.

A PHYSICIAN: What was the clinical diagnosis?

DR. DAVENPORT. Cirrhosis of the liver, with presumable liver abscess because of the fever. The lymph nodes we considered tuberculous—I do not believe we had enough emphasis on the possibility of tuberculous peritonitis.

#### CASE 27442

#### PRESENTATION OF CASE

A forty-three year old Negro stableman was admitted to the hospital because of severe pain in his chest for about twelve hours.

The patient had been well until about three months before entry, when he developed a cough that was productive of blood stained sputum. The

cough was painless, and was always more severe at night, after he had gone to bed. After a month, the sputum ceased to be blood tinged, and remained yellow and purulent.

The patient was free from other symptoms until the night before entry, when, while sitting in front of his barn, he was attacked quite suddenly by pain in the left side of his chest. The pain was sharp, severe, and so aggravated by breathing that he dared scarcely to inhale. He took some whiskey to ease the pain, and went to bed. He slept for a while, only to awake with a similar pain in the right chest. Later in the night, he sweated profusely and had a frank, shaking chill. The next morning, he entered the hospital in considerable distress, complaining of pain on both sides of the chest.

While the patient was a child, both his parents had died of tuberculosis. He had followed race horses all his life, living in or near stables. Twenty years before entry, he had received a large knife wound in the right upper arm. Syphilis was denied, but he had received arm and hip "shots" for a "cold" the winter before entry.

In the three months preceding admission, he had lost 15 pounds.

On examination the patient appeared well developed and well nourished despite some recent weight loss. The expansion of his chest was limited bilaterally. There was occasional coughing, brassy in character. Loud friction rubs were heard over the lower half of each lung field. Breath sounds were definitely diminished in the left chest, although tactile and vocal fremitus were normal, and there were no changes to percussion. The heart did not seem enlarged. The blood pressure was 140 systolic, 90 diastolic.

The temperature was 101°F., the pulse 104, and the respirations 28.

The blood showed a red-cell count of 3,190,000, with 11 gm. hemoglobin. The white-cell count was 14,750 per cu. mm., with 85 per cent polymorphonuclears. The blood Hinton and Wassermann reactions were both positive. Repeated blood cultures were negative. The urine was not remarkable. Numerous examinations of the sputum failed to reveal tubercle bacilli or fungi. On one occasion, a Type 3 pneumococcus was isolated.

A roentgenogram of the chest showed slight enlargement of the heart, affecting especially the left ventricle. At the junction of the ascending portion and arch of the aorta, there was a multilobular dilatation, which seemed to compress slightly the left main bronchus. There was mottled consolidation in the left lower lobe of the lung, in the lower half of the right upper lobe

and in the right lower lobe. The left upper lobe seemed emphysematous. There was no free pleural fluid. The patient was given sulfathiazole and later switched to sulfapyridine. The temperature continued to fluctuate daily from 99 to 102 or 103°F., but the pain disappeared and the cough improved. Early in the fourth week of his hospital stay, severe pleuritic pain in the left chest reappeared for a few days. Re-examination showed dullness in the left axilla and at the left base, with diminished breath sounds. A patch of tubular breathing was present at the left base anteriorly. After this, the patient was given potassium iodide in daily doses, and weekly injections of bismuth.

Another roentgenogram of the chest, taken a month after the earlier film, showed several cavities in the left lower lobe, with fluid levels. The area of infraclavicular consolidation had increased and seemed to include a small cavity.

Bronchoscopy was performed late in the sixth hospital week. The left main bronchus was narrowed and edematous at the orifice, with a considerable amount of thick, gelatinous mucoid secretion. The bronchus to the left lower lobe was narrowed, and contained similar mucoid secretion. A biopsy of the mucosa of the left main bronchus showed no diagnostic abnormality. A roentgenogram of the skull showed no evidence of intracranial metastatic lesions.

On the fifty-ninth hospital day, without premonition, the patient suddenly had a massive hemoptysis, spraying blood all over the room. His mouth and nose filled with frothy clot, and he became pulseless and expired.

#### DIFFERENTIAL DIAGNOSIS

DR. EDWARD F. BLAND: This was a dramatically fatal illness, so far as I can judge from the record, extending over a period of only five months. In exploring the various possibilities, I think we must keep in mind what to me seem to be the essential features of this illness, namely, a progressive subacute pneumonic process in both lungs leading to abscess formation, cavitation and terminal erosion of a large arterial vessel. The diagnostic problem concerns the specific etiologic agent involved, and I hope for considerable help from the X-ray Department on this point. There are two specific questions I should like to ask the roentgenologist. I am bothered by the term "multilobular dilatation" of the aorta. I should like to clear that point up, because most syphilitic alterations in the aorta result in either a diffuse dilatation or a saccular aneurysm. Secondly, does Dr. Lingley find any evidence in the films to indicate osteomyelitis of the thoracic cage?

DR JAMES R LINGLEY There are a number of films, taken over an interval of five weeks. The first film shows widening of the superior mediastinum, which was due to enlargement of the aorta. In the lateral view, one can see marked anterior bulging of the ascending portion and also dilatation of the upper part of the descending portion of the aorta, producing much compression and narrowing of the left main bronchus. The ascending aorta is definitely dilated in a fusiform manner and also shows localized bulges—hence the term ‘multilobular dilatation’. The lesion in the descending aorta is a sacular aneurysm. The process in the lungs at the first observation consisted of a bilateral mottling most evident on the left side at the base and on the right in the midchest and upper chest. During the period of observation, this changed considerably. The process at the left base increased markedly over a period of five days, while the process in the right upper diminished. The patient then developed a new process in the left upper lung followed at a later period by cavity formation both here and in the area of consolidation at the left base. The thoracic cage appears normal.

DR BLAND Now that I have seen the films, I am willing to accept the x-ray interpretation of multiple aneurysmal dilatations of the aorta. Of more importance are the pulmonary lesions. We are dealing with a Negro, and the first thing that comes to my mind is “galloping consumption”. There is, however, some very good bacteriologic evidence against it, so much so that I doubt if this patient actually had tuberculosis. In the first place, with an acid fast bronchopneumonic process of this extent, it is usually relatively easy to demonstrate bacilli in the sputum. I am sure that a very thorough search was made for these organisms, and I am reasonably certain, since this man was on the ward here, that the study included repeated examinations of the gastric contents.

DR TRACY B MALLORY It did.

DR BLAND Furthermore, it is probably true that the material was not only examined but also injected into suitable animals.

DR MALLORY Guinea pig inoculation was done, but no report was available at the time of the patient's death.

DR BLAND Nevertheless, I think the strong, but of evidence, and in fact the only evidence, against tuberculosis is that the organism in this very active process was not demonstrated. Secondly, the lesions here are predominantly at the base of the lungs, that is somewhat against tuberculosis. Finally, I think there are two clues in the clinical record indicating that those in charge

of the patient discarded the idea of tuberculosis—they treated him with iodides—consequently, they must have had some other etiologic factor in mind at that point, also, the patient was bronchoscoped. Ordinarily, in the presence of an active tuberculous process, one does not administer iodides nor does one like to bronchoscope the patient, unless there are very special indications for the latter procedure. Adding up this evidence, then, I shall have to discard tuberculosis.

Next, in searching for other possibilities, I am rather impressed by the fact that three times in the record we are told that this man was closely associated with horses and stables. The Pathology Department in these exercises does not usually stress such possible clues so persistently, therefore, I suppose I should pay special attention to them. Following this lead, the first thing to think of is mycotic infection of the lung. By that term, one means a variety of infections in the lung due to fungi, molds and yeasts. The commonest fungous infection among people who deal with animals and stables is actinomycosis. When the lung is involved, there are often lesions of the skin or subcutaneous structures, not infrequently resulting in draining sinuses. We have no evidence of such lesions here, and Dr Lingley has pointed out that there was no rib involvement. On the other hand, approximately 15 per cent of actinomycosis in human beings may be limited to the lungs. In others, it may be limited to the gastrointestinal tract. It is of some interest that most people believe infection takes place not by direct contact with infected animals or by eating the meat of such animals, but rather from the handling of hay and grain. I hope Dr King will correct me if I have made any misstatements in this connection, for I naturally do not feel so much at ease in dealing with the lungs as with the heart. In considering actinomycosis as possibly responsible, I am a little bothered that the ribs were uninvolved, and that there were no draining sinuses. I am also further disturbed by the fact that they were not able to demonstrate the organism either in the sputum or in the material that came from the bronchoscopic examination, but this does not exclude actinomycosis. On the other hand, the somewhat chronic course with hemoptysis and cavity formation is a part of the general clinical picture of mycotic infection of the lung, especially actinomycosis. The mucoid character of the sputum is fairly characteristic. Another point somewhat against it is that the patient presumably did not respond to chemotherapy. However, I do not believe we have had enough experience with chemotherapy in mycotic infections to assess this

evidence one way or the other. There are several reports pointing out that some patients do respond favorably. We also do not know how much chemotherapy was actually given. Perhaps there was some special reason for switching from sulfathiazole to sulfapyridine and then omitting it entirely. Perhaps they were never able to get the blood level high enough, but we can only speculate about that. I must say that since acid-fast bacilli could not be found I view with favor the possibility of actinomycosis.

In searching for other possibilities in a person associated with stables, one thinks of tetanus. There is no place here for tetanus that I can see. Then we think of anthrax. There are reported cases of pulmonary anthrax, a rapidly fatal disease; the patient usually dies in a few hours or a day or two and actually often before physical signs are demonstrable in the lungs. Finally, there is the possibility of glanders in the lung; but that would be a little fanciful here.

Another condition one must think of as a cause of subacute or chronic pulmonary consolidation is Friedländer's pneumonia. About 3 per cent of pneumonias are due to the gram-negative encapsulated Friedländer's bacillus. It is usually acute, lasting something like eight to fourteen days; but now and then it may be a more chronic process such as this patient showed, and it is often associated with hemoptysis, consolidation and multiple cavitation of the lung—the result of a non-putrid pulmonary necrosis. The sputum is often mucoid, but I am also disturbed here by the fact that the organism could not be demonstrated. There is no specific statement in the record concerning Friedländer's bacillus; it would have been mentioned if found. Therefore, I think that this was not Friedländer's pneumonia.

Is there any possibility of neoplastic disease, either primary or secondary, carcinoma or lymphoma? I do not believe so. The x-ray report does not suggest it. The bronchoscopic examination simply shows narrowing of the left main bronchus, probably from external pressure of the dilated aorta, possibly in part from chronic inflammatory swelling inside the air passage itself. Biopsy of this area failed to reveal evidence of cancer.

We know that the patient had syphilis. Can we bring syphilis into the picture otherwise than by its probable involvement of the aorta? Syphilis of the lung itself is rare. Cases of gumma have been described, and have been seen here in this hospital. This patient was treated with iodides and bismuth, not, I suppose, because anyone thought there was syphilitic involvement of the lung but rather because the patient had positive

serologic findings and a large aorta. Rarely, syphilis may involve the pulmonary artery, usually with aneurysmal dilatation, or very occasionally as a form of endarteritis of the smaller radicles but I see no evidence for suspecting such a diagnosis here.

Did the patient inhale a foreign body caused obstruction, secondary infection and bronchiectasis? There is no evidence to suggest from the history or subsequent course.

I keep asking myself whether we are trying to make this case too complicated. Was this, after all, simply bronchiectasis of the lung present long time and more or less latent until the terminal infection? There were no symptoms in the past to suggest such a process. They are always necessary. Perhaps bronchiectasis under pressure by the aneurysm on the left main bronchus, with secondary infection behind it that spread to the other lung, is a possibility. I do not see how we can say yes or no. I am inclined to think that there was some specific infectious cause of this lung other than simple mechanical obstruction of the bronchus and trapped infection.

After exploring these various etiologic possibilities, I can briefly summarize by saying that I am back to where I started. The evident diagnosis is that of a bilateral pulmonary infection with multiple abscess formation and cavitation of undetermined etiology, in addition to a question of actinomycosis. The patient undoubtedly had syphilis, with aneurysmal dilatation of the aorta. Then there was the terminal pulmonary hemorrhage. Obviously, a large vessel was eroded. Was it the aorta? Was it rupture from pressure within, was it aggravated by weakening of the wall of the vessel from without, or was it simply an erosion of a large pulmonary vessel? I do not know how we can decide. My impression is that rupture of the aorta leads to rather instantaneous death. In this case, those who saw the patient had time to make a few observations. They did not say whether the blood was bright red or dark red, suggesting it might have been from the aorta in the first event or from the pulmonary artery in the second. I do not know how we can decide where it came from, but certainly it was from a large arterial vessel.

DR. DONALD S. KING: We saw this patient several times in the Thoracic Clinic. At first agreed with the student who took the history that the diagnosis was pulmonary tuberculosis, but we were baffled by the repeated negative sputum examinations, and began to look for other possible etiologic factors. Because of his association with horses, we thought, as Dr. Bland did, of ac-

mycosis, but could never prove it. In speaking of actinomycosis, it might be well to note that the disease may develop in city dwellers who have had no contact with animals. We recently had such a case in a young female stenographer. In the present case, we thought also of Friedlander's infection, but could not find the organism. We then got interested in the possibility of pulmonary syphilis and agreed with the recommendation that antisyphilitic treatment be tried.

Dr Bland raised the question of bronchoscopy in cases of pulmonary tuberculosis, and I should perhaps say that, at times, even with acute pulmonary tuberculosis, bronchoscopy is indicated. We are coming to recognize bronchial tuberculosis as a fairly common complication. An acute bronchial obstruction from tuberculous infection may have to be relieved by the bronchoscopic procedure. If proper drainage can be established, fever and other untoward symptoms may be promptly relieved. In the present case, if there was definite evidence of obstruction to the left lower lobe bronchus, bronchoscopy was justified, even though there was the possibility of the diagnosis of tuberculosis.

Dr Lingley, if you saw this x-ray film and did not know the story, would the diagnosis be evident?

Dr LINGLEY. The x-ray appearance would fit actinomycosis very well, in spite of the lack of rib destruction. It is unusual for tuberculosis to be at the base predominantly and for the consolidation to fluctuate so much. I do not know of any positive method of making a diagnosis of syphilis of the lung, although various criteria have been suggested. I think actinomycosis is as good as anything.

Dr KING. Would you have guessed that if you had seen the film?

Dr LINGLEY. Chronic pulmonary infection with cavitation is as far as I can go on the films alone.

Dr KING. I know the diagnosis now, but as I see the films from here it seems that we should have made the diagnosis from them. The fact that the process was predominantly basal does not rule out tuberculosis. There also was bilateral apical infection.

Dr BLAND. What was the clinical diagnosis on the death report?

Dr MALLORY. Chronic pulmonary suppuration, tertiary syphilis, with aortic aneurysm and terminal rupture into a bronchus.

Dr BLAND. Where did you think the terminal hemorrhage came from?

Dr KING. I know the autopsy findings, but I think that the service made the correct diagnosis.

#### CLINICAL DIAGNOSES

Chronic pulmonary suppuration  
Tertiary syphilis, with aortic aneurysm and terminal rupture into a bronchus

#### DR BLAND'S DIAGNOSES

Chronic pulmonary infection of undetermined etiology (actinomycosis?)  
Multiple pulmonary abscesses  
Tertiary syphilis  
Aortic aneurysms  
Terminal hemorrhage

#### ANATOMICAL DIAGNOSES

Syphilitic aortic aneurysms (three), with rupture of one into the left lower bronchus  
Hemorrhage into lung  
Syphilitic aortitis  
Compression of left bronchus by aortic aneurysm  
Pulmonary tuberculosis, bilateral, with cavitation  
Secondary erosion of vertebral bodies by aneurysmal dilatations

#### PATHOLOGICAL DISCUSSION

Dr MALLORY. The autopsy showed marked dilatation of the aorta, with multiple aneurysms, two of which were definitely saccular, the third being a more diffuse dilatation. The larger aneurysms were found in the ascending portion, and the smallest aneurysm was just beyond the arch in the descending portion. It had become adherent to the left primary bronchus and had ruptured into it terminally; death was due to the inhalation of tremendous amounts of blood throughout the bronchial tree and even into some of the alveoli. The patient essentially drowned in his own blood rather than dying of hemorrhage. The pulmonary picture was somewhat confused from the gross point of view by the massive inspiration of blood, but many areas of consolidation were found scattered throughout all lobes of the lung, some of which showed varying degrees of caseous softening and some frank cavitation. On gross examination, it was not recognized as tuberculosis, but on microscopic examination it was perfectly obvious. Eventually, the guinea pig that had been inoculated with the gastric contents was found to show tuberculosis. The heart itself was not involved in the aortic process. The lesion was too high to affect either the aortic valve or the coronary ostia.

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THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

## AMERICAN COLLEGE OF SURGEONS

FROM November 3 through November 7, the surgeons of Metropolitan Boston will be hosts to the clinical congress of the American College of Surgeons, with headquarters at the Hotel Statler. These annual meetings are among the greatest and most effective educational gatherings that are held by any branch of the profession. The surgeons of the large local hospitals will demonstrate their methods and ability, and many distinguished visitors will give addresses or take part in the discussions. Among the guest speakers will be Dr. Evarts A. Graham, of St. Louis, the president of the college, and Dr. W. Edward Gallie, of Toronto, the president-elect. From abroad will come Rear-Admiral Gordon Gordon-Taylor, of London, and Professors Pablo Luis Mirizzi, of

Cordoba, Argentina, and Moacyr Eyck Alvaro, of Sao Paulo, Brazil.

In addition to surgical clinics, round-table conferences and scientific meetings in the daytime, the Presidential Meeting and Convocation is scheduled for Monday evening, and formal scientific lectures for the following three evenings. On Friday evening, the Boston Surgical Society will hold a special meeting, at which Dr. Allen O. Whipple, of New York City, will be awarded the Bigelow Medal.

Matters pertaining to hospital standardization will be discussed at meetings held at the Copley-Plaza. These gatherings should be of interest to physicians, hospital executives, nurses and laymen, and particular emphasis will be placed on proper systems for the making-out and filing of hospital records.

Admission to the clinics and surgical round-table conferences will be by ticket only, to prevent overcrowding. For members or junior candidates of the College, the registration fee is \$5.00, payable at the registration desk at the Hotel Statler; candidates accepted by the College for induction at this meeting may register without charge. For nonfellows attending the congress as invited guests of the College, the registration fee is \$10.00. No fee is involved for attendance at the meetings concerned with hospital standardization, but all who plan to be present should register at the desk at the Copley-Plaza.

## NUTRITION AND DEFENSE

THE old adage, "An army travels on its stomach," might well be changed to "A nation travels on its stomach." There was a time when the fighting of wars did not greatly disturb the activities of much of the populace. But times have changed. World War II gives ample demonstration that efficiency and morale on the home front are as essential for winning wars as fighting on the battlefield. Warfare has so changed that millions of workers behind the lines are required for the continued delivery of supplies and mechanical equipment to the fighters. There is a

considerable medical literature to attest that malnutrition in its various forms impairs this physical efficiency and morale so essential to victory

A recent study by Williams and Mason\* adds convincing evidence for this contention. These investigators placed a number of healthy adults on a diet adequate in all respects but with a thiamin content of only 0.40 to 0.45 mg daily. They point out that this approximates the thiamin content found by Stebeling and Phipard in the diets of many American families. After four to six months, in addition to other manifestations, these subjects became depressed, irritable, quirkish, fearful, inefficient in work because of generalized fatigue, inattentive to details, uncertain of memory and lacking in manual dexterity. These symptoms slowly disappeared when additional thiamin was added to the diet. This is a convincing demonstration of the necessity of thiamin for emotional stability. Indeed, thiamin has been referred to in the lay press as the "morale vitamin," and people in the occupied countries are said to be more easily kept in a subjugated state because the low thiamin content of their diets has robbed them of their will to fight.

Thiamin, however, is only one of the many factors that may be absent in a poor diet. At the National Nutrition Conference for Defense, held in Washington this May at President Roosevelt's request, the frequent inadequacy of the American diet was frankly discussed. Specific recommendations for improving the nutrition of the people were made to the President. The exigencies of the hour necessitate that the advantages to accrue from the application of nutritional principles to defense efforts begin as soon as possible. Aside from these immediate objectives, the nutritional program now getting under way in this country has far-reaching implications and may materially influence the pattern of morbidity in the generations to come. At the conference, all physicians were urged to take an active interest in these nutritional problems and to assume leadership in the field. The progress report in this

issue of the *Journal* reviews material with which every physician should be familiar.

## MEDICAL EPONYM

### KRONIG'S ISTHMUS

Dr Georg Kronig (1856-1911), docent in the University of Berlin, published his paper "Zur Topographie der Lungenspitzen und ihrer Percussion (On the Topography and Percussion of the Lung Apices)" in the *Berliner klinische Wochenschrift* (26: 809-812, 1889). A portion of the translation follows:

The examination of a patient who had been referred to me was the beginning of a series of determinations of the borders of the lung apices, as well as the lung margins which I briefly report here. After I had determined the anterior supraclavicular margin of the lung in the usual fashion, that is by gentle percussion, I proceeded, still percussing very lightly to the posterior aspect and thereby obtained the following results. On the right side, as on the left, there appeared a line that extended medially in a wide arch, with its convexity directed inward, and approached to within a centimeter of the midline on the left at the level of a line between the second and third thoracic spines, on the right at the level of the fourth thoracic spine. In this case, the right apex was diseased while the left showed a normal condition. Inasmuch as I had obviously been successful in determining not only the height of the lung apices but also their breadth, I tried to determine similarly the lateral margin. The determination of the posterior lateral border is easy in many cases, especially in thin persons, but is frequently difficult in powerfully built, extremely muscular, or fat persons. The lateral border, which I have outlined on the anterior surface is extremely trustworthy. It runs from about the middle of the anterior margin of the trapezius muscle, curves down sharply, cuts the clavicle at about the line between its middle and outer third, and then courses outward diagonally to the axilla. From the configuration of these normal clinical margins, it will now be possible, without great difficulty, to hypothesize the necessary shift that will occur when there are pathologic changes in the lung apices. Diseases that reduce the air content will shift the medial border outward and the lateral border inward.

R W B

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY†

#### AIR ENBOLUS FOLLOWING AN ATTEMPT AT CRIMINAL ABORTION

As in so many cases that the medical examiner sees, no record of the past history or physical ex-

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr Raymond S. Titus, Secretary, 340 Dartmouth Street, Boston.

\*Williams R O and Mason H L. Further observations on reduced thiamine (vitamin B<sub>1</sub>) deficiency and thiamine requirement of man. *Proc Soc Exp Biol Med* 1941; 48: 433-435.

amination was available for the following case. According to the meager history obtained, the patient was single, twenty-two years old and about eighteen weeks pregnant. She went to a female abortionist, who attempted to bring about an abortion by the use of a large bulb syringe. The patient died almost immediately. Autopsy revealed air embolus in the heart and in the lungs.

*Comment.* This case is reported solely because of the rarity of such a cause of death, proved by autopsy. Each year since the Maternal Mortality Study was begun, 25 to 30 fatal criminal or self-induced abortions have been reported in Massachusetts. That the above-mentioned abortion was performed in such a manner by a female abortionist probably relieves the medical profession of any responsibility. The danger of this method of abortion must be so well known to the profession that it is doubtful whether any registered physician would attempt it.

## DEATH

MASON—ATHERTON P. MASON, M.D., of Fitchburg, died October 20. He was in his eighty-sixth year.

A native of Fitchburg, Dr. Mason received his degree from Harvard Medical School in 1882. He was a former president of the Worcester North District Medical Society, and was a member of the Massachusetts Medical Society and the American Medical Association.

He is survived by a daughter.

## NOTICES

### JEWISH MEMORIAL HOSPITAL

A diagnostic therapeutic conference will be held at the Jewish Memorial Hospital on Thursday, November 6, at 11 a.m. Dr. Valy Menkin will discuss "Inflammation."

Interested physicians and medical students are cordially invited to attend.

### MASSACHUSETTS PSYCHIATRIC SOCIETY

The annual meeting of the Massachusetts Psychiatric Society, with the election of officers, will be held at the University Club, Boston, on Friday, November 7, at 6:30 p.m. The guest speaker will be Dr. Winifred Cullis, professor emeritus of physiology, University of London, whose topic will be "London Hospitals in Wartime."

### NEW ENGLAND OTO-LARYNGOLOGICAL SOCIETY

The fall meeting of the New England Oto-Laryngological Society will be held at the Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston, on Wednesday, November 19, at 4:30 p.m. The clinical meeting will be followed by a buffet supper.

### NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children

will be held on Thursday, November 6, at 7:15 p.m. in the classroom in the nurses' residence. A motion picture, "Studies in Human Fertility," will be shown. Dr. Mary I. Tompkins will be chairman.

### AMERICAN ORTHOPSYCHIATRIC ASSOCIATION

The nineteenth annual meeting of the American Orthopsychiatric Association will be held at the Hotel Statler, Detroit, Michigan, on February 19, 20 and 21.

A registration fee will be charged for nonmembers. Further information may be obtained from Dr. Helen P. Langner, chairman, Publicity Committee, Vassar College, Poughkeepsie, New York.

### CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Salem	November 3	Paul W. Hugenberger
Lowell	November 7	Albert H. Brewster
Haverhill	November 12	William T. Green
Brockton	November 13	George W. Van Gorder
Pittsfield	November 17	Frank A. Slowick
Northampton	November 19	Garry deN. Hough, Jr.
Worcester	November 21	John W. O'Meara
Fall River	November 24	Eugene A. McCarthy
Hyannis	November 25	Paul L. Norton

### SOCIETY MEETINGS AND CONFERENCES

#### CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, NOVEMBER 2

##### MONDAY, NOVEMBER 3

American College of Surgeons Statler and Copley Plaza hotels  
12 15-1 15 p.m. Clinicopathological conference Peter Bent Brigham Hospital amphitheater.

##### TUESDAY, NOVEMBER 4

American College of Surgeons Statler and Copley Plaza hotels  
12 15-1 15 p.m. Clinicorontogenological conference Peter Bent Brigham Hospital amphitheater.

##### WEDNESDAY, NOVEMBER 5

American College of Surgeons Statler and Copley Plaza hotels  
\*12 00 m. Clinicopathological conference. Children's Hospital

##### THURSDAY, NOVEMBER 6

American College of Surgeons Statler and Copley Plaza hotels  
\*8 30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Peter Bent Brigham Hospital Conducted by Dr. Soma Weiss  
\*11 00 a.m. Inflammation. Dr. Valy Menkin Jewish Memorial Hospital  
7 15 p.m. New England Hospital for Women and Children. monthly clinical conference and meeting of staff

##### FRIDAY, NOVEMBER 7

American College of Surgeons Statler and Copley Plaza hotels  
6 30 p.m. London Hospitals in Wartime Dr. Winifred Cullis Massachusetts Psychiatric Society. University Club, Boston

\*Open to the medical profession

OCTOBER 31-JANUARY 30 Massachusetts General Hospital. Clinical staff meetings of the Children's Medical Service. Page 673, issue of October 23  
OCTOBER 31-APRIL 24 Massachusetts Memorial Hospitals. Staff meetings Page 672, issue of October 23.  
NOVEMBER 3-7. American College of Surgeons. Page vii, issue of July 31  
NOVEMBER 4 Portsmouth Naval Hospital Page 673, issue of October 23  
NOVEMBER 5-6 American Conference on Industrial Health Page 473  
\*issue of September 18  
NOVEMBER 13 Pentucker Association of Physicians  
NOVEMBER 17-19, 21-22, 27 and 30 Thomas William Salmon Memorial Lectures Page 636, issue of October 16  
NOVEMBER 19 New England Oto Laryngological Society Notice above



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## SYMPOSIUM ON HORMONES

### COMPLICATIONS OF THYROID-SUBSTITUTION THERAPY\*

WILLIAM T. SALTER, M.D.†

BOSTON

Preparations of endocrine glands in the form of crude extracts or purified synthetic active principles may be classified from a pharmacological viewpoint as drugs of animal origin. Whereas most drugs are substances foreign to the body, the hormones are normally present and active in tissues where they have a physiological function. For this reason there is some tendency to place hormones in a different category from drugs. There is no valid reason for this, however, and indeed the older endocrine preparations have unobtrusively broken down this arbitrary distinction. For example epinephrine is much more frequently viewed as a powerful sympathomimetic drug than as the hormone of the adrenal medulla.

The fact that the drugs of endocrine origin do have a physiological function has aided considerably in the elucidation of their mechanisms of action. A drug foreign to the body can only be studied with respect to its positive effects after administration. Observations on the response to a deficiency or an excess of a hormone can be made both in the clinic and in the laboratory. With this dual investigative method, much has been learned concerning the mechanisms of action of the hormones. Despite the extensive physiological and pharmacological evidence available, the endocrine preparations are probably more often misused in therapy than any other group of drugs. Extravagant claims are often made for their efficacy, and they are widely employed in conditions entirely unrelated to hormonal deficiency. Routes of administration are frequently used which preclude the possibility of obtaining pharmacodynamic action. Rational therapeutic employment of drugs of endocrine origin clearly depends on a thorough knowledge of their chemistry, and of their physiological and pharmacological actions.

Goodman and Gilman<sup>1</sup>

**A**LTHOUGH thyroid substitution therapy is one of the best known and most reliable types of endocrine treatment, a number of features concerning it are apt to be overlooked in the course

of a busy practice. These involve not only certain therapeutic hazards that attend the use of this medication, but also neglected opportunities for permanent good. The thyroid hormone has two main effects: first, that of growth and maturation and, secondly, that of the release of energy. The physician must take advantage of these properties, while avoiding their undesirable features. In this respect, the wise use of thyroid medication requires a considerable acquaintance with the art of medicine.

#### TYPE OF THERAPY

For most purposes, desiccated thyroid—thyroid *U S P*—is to be preferred to any other type of thyroid preparation, because in general it is cheaper and because its assimilation is better assured. Thyroxin crystals are so insoluble that they may pass through the gastrointestinal tract with little if any absorption, and at best the degree of absorption is frequently unreliable, even when the crystals are administered in solution. Therefore, thyroid *U S P* should ordinarily be given only by the parenteral route, either when difficulty in absorption by the intestine is anticipated or when, for scientific or other reasons, it is desirable to know definitely how much of the drug reaches the circulation. Such conditions might involve massive edema of the intestine, ulcerative lesions or even steatorrhea. Likewise, very rarely, protein sensitivity may lead to allergic symptoms like urticaria, which preclude the use of glandular preparations. If thyroxin is given, it should be dissolved in dilute alkali (N/100) and further diluted (N/1000) just before injection. Ordinarily, however, both for the treatment of frank myxedema and for other therapeutic purposes, one should employ desiccated thyroid, usually in tablets containing 1 gr. (60 mg.) of the material, commonly given twice daily.

\*This and the three subsequent papers were presented as part of a symposium at the annual meeting of the Massachusetts Medical Society, Boston, May 22, 1941.

From the Thorne Medical Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School, Boston.

†Formerly assistant professor of medicine, Harvard Medical School, and associate physician, Thorne Medical Laboratory, and junior visiting physician, Boston City Hospital.

## THERAPEUTIC HAZARDS

In the treatment of myxedema, care must be exercised, particularly in older people, lest the reserve of certain organs be overtaxed. These include especially the heart and the adrenal cortex. The danger of precipitating acute dilatation of the heart, with left-sided failure, acute pulmonary edema, anginal seizures and even coronary thrombosis, has often been commented on,<sup>2</sup> and need not be amplified further. Less well known is the precipitation of acute shock, Addisonian in type, in a disorder that Means et al.<sup>3</sup> have classified as "hypothyroidism masquerading as myxedema." Many endocrinologists would consider this type an early stage of Simmonds's cachexia, in which thyroid lack had become more prominent than disturbances in the other endocrines. Such cases, however, can be verified properly if special attention is paid to points in the history that suggest hypogonadism and the symptoms and signs of Addison's disease. The presumptive diagnosis can be verified by the appropriate use of insulin-tolerance and glucose-tolerance tests.<sup>4</sup> Obviously, such a case must be treated with thyroid only under hospital control and with extreme care.

The dosage tolerated by a patient with classic myxedema varies with the patient's age. Many young patients (under twenty years of age) tolerate without difficulty as much as 4 gr. a day of thyroid *U. S. P.*, although this dosage is not to be recommended routinely. On the third to the fifth day of treatment, they may experience a certain amount of mild fever and muscle pain of minor character; otherwise, little discomfort results. Under such dosage, the patient's metabolism usually reaches -10 per cent in two weeks, and if the dosage is continued, it slowly rises to normal in a month after the beginning of therapy. Older people must be treated more cautiously, even in the absence of definite heart disease. Thyroid is in itself, of course, a diuretic, and at all levels of metabolism will produce a certain degree of diuresis unless heart failure is precipitated, when the diuresis may be masked by increasing edema due to heart disturbance.

As pointed out by Goodman and Gilman<sup>5</sup> and others,  $\frac{1}{2}$  gr. a day will, in the course of a month, bring the metabolism up to -35 per cent, 1 gr. to -25 per cent, 2 gr. to -15 per cent, and 3 gr. to -10 per cent. Equivalent dosage for thyroxin has been given by Thompson and his associates.<sup>6</sup> With this approximate scheme in mind, one may start in with  $\frac{1}{2}$  gr. a day for ten days, and slowly elevate the dosage each week as required. Usually, not more than 2 gr. (120 mg.) daily suffices.

Some patients must be content with a subnor-

mal level because their hearts do not tolerate a normal metabolic rate without the onset of cardiac failure or of angina pectoris. In general, the basal metabolic rate may be as low as -20 per cent before the layman can detect a difference in the patient's appearance or personality. Indeed, the patient sometimes prefers this level because he finds life far less worrisome.

In cretins, adjustment of the dose is particularly precarious because there seems to be a rather narrow margin of safety between an inadequate dose and one that produces violent mental symptoms.<sup>7</sup> Indeed, in untreated cretins over fifteen years of age, there is a prevailing sentiment that treatment may often be worse than useless because it merely makes the patient unhappy and intolerable to other members of society. In juvenile myxedema, this limitation is less disturbing, and for the sake of the general development and growth of such young people, it is desirable to run them constantly with a somewhat elevated metabolism. In fact, it is surprising how content very young people can be for long periods with a basal metabolic rate that is close to +20 per cent. Accordingly, children often well tolerate doses ordinarily given to adults.\* On the contrary, an old person frequently complains bitterly at a level of +5 per cent.

If dosage is pushed too high in women in the childbearing age, scanty or irregular menstruation may result. On the other hand, thyroid therapy in mild myxedema may correct menorrhagia and metrorrhagia; and in profound myxedema, minimal thyroid therapy may initiate regular menstrual periods that have been stopped for some years because of thyroid lack.<sup>9</sup> One thus sees a reversal of the effect of thyroid on menstruation, that is, no periods at a basal metabolic rate of -45 per cent, menorrhagia at -20 per cent, oligomenorrhea at +15 per cent and, possibly, no periods at +50 per cent.

Even when too little thyroid secretion is present, as in myxedema, the patient may complain of nervousness, and occasionally hyperthyroidism may be suspected. This paradoxical nervousness or irritability of the hypothyroid patient may be a frustration complex analogous to that shown by older men engaged in mass production who are no longer able to maintain the speed of the assembly line. These myxedematous patients are

\*Means<sup>3</sup> has recommended the following dosage of thyroid *U. S. P.* in the treatment of cretins:

AGE	DAILY DOSAGE
2 to 4 mo.	6 mg. (1/10 gr.)
4 to 8 mo.	12 mg. (1/5 gr.)
8 to 12 mo.	18 mg. (3/10 gr.)
12 to 24 mo.	24 to 45 mg. (2/5 to 3/4 gr.)
2 to 4 yr.	30 to 90 mg. (1/2 to 1 1/2 gr.)
4 to 12 yr.	60 to 180 mg. (1 to 3 gr.)

usually content until their neighbors begin to push them, when they become harassed and irritable. With moderate thyroid dosage, they live faster and can maintain the pace of modern life. On the other hand, excessive overdosage may lead to violent maniacal attacks, accompanied by a flight of ideas and even incoherent bawling, with intermittent echolalia, babbling and other psychic phenomena. In general, these attacks are likelier to be precipitated by rapid elevation of the basal metabolic rate than by slow elevation. Of course, myxedematous patients are more sensitive to high doses of thyroid than persons whose glands are normal.

Other bodily functions may be accentuated unpleasantly by overdosage of thyroid. Among these abnormalities are diarrhea produced by increased thyroid activity, excessive sweating, palpitation and restlessness to the point of apprehension. Occasionally, particularly in older people, auricular fibrillation may be precipitated by the use of too much thyroid, and normal cardiac rhythm may be resumed when this medication is stopped. This phenomenon is not infrequently encountered in weight reduction, when an overenthusiastic patient "doubles the dose." In the absence of frank circulatory or arteriosclerotic disease, and in the presence of a normal thyroid gland, it is probably rare to see very alarming symptoms until the dose exceeds 2 gr. (120 mg.) a day. In general, of course, the same rule holds for thyroid as for many other drugs, namely, that the law of diminishing returns applies. If the patient is truly hypothyroid, a relatively small dose will produce a marked effect on the metabolic turnover, whereas if the patient is suffering from reduced metabolism due to some other cause, rather large doses may be required to produce any considerable effect on the metabolic rate. Indeed, some clinicians go so far as to say that there is little point in giving over 3 gr. (180 mg.) daily.

This therapeutic test may be applied in cases of nephrosis and of hypogonadism (hypopituitarism) or in cases of so called "substandard" (but normal) basal metabolic rate. This last group is particularly interesting because it comprises that end of the distribution of the healthy population whose basal metabolism under normal conditions happens to lie between -15 and -25 per cent. Such cases are not infrequently branded as hypothyroid on the basis of the metabolic rate determination, and treated unnecessarily. Indeed, they may erroneously be called "myxedema," when actually that term should be reserved for the characteristic clinical syndrome recognizable at the bedside. In case of doubt, chemical determination

of the plasma protein bound iodine<sup>23</sup> is a highly reliable confirmatory test.

In the minor degrees of true hypothyroidism, however, the patient may often be benefited symptomatically by thyroid, and the experienced practitioner is justified in trying the therapeutic effect in certain cases of borderline endocrine imbalance in which mild stigmas of thyroid underfunction seem to be prominent. This is true even though the basal metabolic rate lies within normal limits. Occasionally, although somewhat uncommonly, doses as high as 5 gr. a day may be necessary in young people. Farquharson and Squires<sup>10</sup> have pointed out, however, that when medication is stopped in such patients the basal metabolic rate may fall abruptly to markedly subnormal levels, and that it returns to normal only gradually, even when high calorie diets are supplied.

In other endocrine deficiencies, the use of thyroid may upset the endocrine balance disadvantageously. For example, mild diabetes mellitus may be aggravated,<sup>11</sup> or mild tetany may be enhanced. On the contrary, it is well substantiated that in lack of pituitary or ovarian secretion, thyroid therapy may increase the efficiency of small amounts of growth hormone or gonadotropic hormone reaching the peripheral tissues, and in young, undeveloped patients the use of thyroid alone in rather large doses may suffice to promote adequate growth and maturation. Such therapy, of course, should be persisted in only after chronic systemic disease, such as tuberculosis or nephritis, has been ruled out, because under such circumstances the increase in caloric turnover would only add insult to injury. Occasionally, in hospital practice, one finds a renal dwarf whose condition has been made worse by an ill founded hope of stimulating growth by thyroid therapy.

In addition to these precautions, there remains a large group of borderline or twilight conditions in which no clean cut syndrome can be diagnosed, but in which the patient responds far more strikingly to thyroid therapy than he would respond to placebos. Such symptoms as lassitude, overweight, inability to think and mild mental depression may in properly selected cases be benefited by thyroid, judiciously administered. Even obstinate constipation, based on mild hypothyroidism, may in itself justify such treatment. The dosage required for this type of therapy is often rather large and should not be persisted in without due precautions. A striking example of the abuse of this type of therapy has been reported by Richardson<sup>12</sup> in anorexia nervosa, a disease that occurs generally in young women suffering from a morbid desire for reduction of weight, even to

the point of emaciation. Because their basal metabolic rate is frequently under -25 per cent, the practitioner is tempted to give thyroid, especially in the hope that it may stimulate appetite. Such therapy only increases the emaciation and the mental agitation of the patient, and may be responsible in part for the not infrequently fatal outcome in such cases.

#### NEGLECTED OPPORTUNITIES

Whenever one encounters a patient suffering from cretinism or juvenile myxedema who has the physical appearance and mental status of a child, although mature in years, one realizes that such a patient represents a gross failure in therapy based on neglect. Such patients are likely to live many decades as a sad reminder of the fact that, had proper treatment been pursued consistently, they might have become useful citizens. In treating cretins or patients with juvenile myxedema, therefore, it is particularly important to begin early and to maintain active therapy continuously for many years. With present-day standards of therapy, however, the cretin has only about an I. Q. of 60, whereas nearly all cases of juvenile myxedema attain this level of intelligence.<sup>13</sup> This difference presumably reflects the lack of iodine or thyroid hormone experienced by the cretin during intrauterine life, as witnessed by the presence of cretinoid goiter at birth. With better therapy, persistently adhered to, Rolleston<sup>14</sup> believes the prognosis to be correspondingly brighter.

All intergrades exist in degrees of thyroid lack, ranging from the striking imbecilic dwarf to young people who do not have quite enough thyroid secretion to enable them to grow up physically and mentally. Some patients with delayed puberty, for example, may require merely extra thyroid hormone to increase their stature and to facilitate sexual maturity. When treated with rather large doses of thyroid for several years, such persons may grow many inches in height and undergo a complete change in personality. Such a case has been reported in detail by Zondek.<sup>15</sup> The obscurity of these early hypothyroid problems is illustrated by a case seen recently at the Boston City Hospital.

A 14-year-old schoolboy was referred for study with a chief complaint of enuresis. The past history was negative except for measles and chicken pox in early childhood. He had always been active and well, although a trifle small for his age and slightly backward in school. His father was somewhat perturbed at his immaturity and lack of interest in the opposite sex.

On physical examination, the patient was found to be poorly developed and moderately well nourished. The

scapulas tended toward the "wing" position. There was moderate left dorsal scoliosis. The external genitalia were those of a boy of 10. The testes were descended, and about 1.5 by 1.0 cm. in size. Pubic and axillary hair was absent. The skin was somewhat dry, but not cold. The pulse rate was 70. The weight was 8 pounds under standard, according to Bardeen's tables.<sup>16</sup> X-ray study showed epiphyseal ossification at least 1 year delayed. The basal metabolic rate was -13 per cent by the Boothby-Sandiford modification of the Dubois standards. The plasma protein-bound iodine was 3.7 microgm. per 100 cc., that is, the level found in incipient myxedema in the adult. The 17-ketosteroid excretion for 24 hours was somewhat subnormal for his age.

The patient was placed on thyroid U.S.P., beginning with  $\frac{1}{2}$  gr. and increasing cautiously to 3 gr. daily. Special care with the diet was advised, and general hygiene instituted.

Obviously, this therapy must be undertaken before the epiphyses have finally closed, and it must be accompanied by appropriate supportive measures, such as general hygiene and good diet, and often with a certain amount of psychiatric or social adjustment. Frequently, too, other hormones may be supplied to advantage, but it is sometimes surprising how much the addition of thyroid alone will accomplish. Thus, Foster and Thornton<sup>17</sup> have successfully used thyroid in the treatment of menstrual irregularity in certain groups of cases. There is ample scientific background for this therapy apart from clinical experience, because it has been demonstrated clearly that the peripheral tissues utilize small amounts of growth hormone<sup>18</sup> and of sex hormone more effectively when adequate thyroid secretion is present. Indeed, hens lay more eggs<sup>19</sup> and cows give more milk<sup>20</sup> under similar circumstances. In the use of such therapy, due consideration should be given not only to the normal growth curve of the patient in question, estimated both in the light of standard statistics, such as those of the standard tables of Bardeen,<sup>16</sup> but also to the patient's forebears.

At present, too much attention is paid to the basal metabolic rate in the control of therapy. This is a useful objective method of deciding whether the patient needs more or less medicine, but the controlling factor ordinarily is the patient's own physiologic state. Barring untoward effects of troublesome degree, the patient should receive enough medicine to rectify the complaint. This is merely common sense, but it is often lost sight of in routine therapy. In general, the more the drug is needed, the lower the dose required to rectify the disorder.

Certain cases of mistaken diagnosis may sometimes be disclosed by a sluggish response to thyroid therapy. For example, loss of hair from natural causes may occasionally be mistaken for evidence of hypothyroidism, or chapping of the skin

and lips in winter due to alkaline soaps or to vitamin deficiency may similarly be misinterpreted. In the dry eczema of old people, however, the so-called "eczema hiemalis," the judicious use of thyroid may lead to increased sweating and secretion of the sebaceous glands sufficient to make tolerable an annoying condition. When such therapy is undertaken in older people, of course, particularly during cold weather, there is always a certain risk of overstraining the heart.

#### NEW PROBLEMS

In recent years, special interest has been focused on cases of Graves's disease without hyperthyroidism, exhibiting the syndrome that Brun<sup>21</sup> has termed "exophthalmic ophthalmoplegia." Such patients as a general rule do not have in abnormally high basal metabolic rate; indeed they may show a subnormal basal metabolic rate, especially if they have been treated previously by subtotal thyroidectomy. A high concentration of thyrotropic hormone is usually found in the urine, unlike that of classic hyperthyroidism. The average surgeon is tempted in such cases to operate a second time and remove more of the gland, but accumulating experience indicates that this merely exaggerates the disturbance. At the present time, one useful method of therapy seems to be that of rather high dosage of thyroid, usually combined with iodine.<sup>22</sup> The large doses of thyroid, of course, elevate the basal metabolic rate, and such patients must pay for the preservation of their eyesight by a certain number of months of artificial hyperthyroidism, exogenous in origin. It may even be necessary to use repeated injections of thyroxin in solution by vein, but this situation is very rare and such treatment should be carried out only in a hospital. Under favorable circumstances thyroid therapy may check the advancing exophthalmos and may eventually lead to satisfactory recession of the globe. In the course of such a program, due consideration must obviously be given to the cardiac status and similar variables. In my experience in a large hospital, this group has comprised over one tenth of the cases in which the thyroid status has been questioned.<sup>23</sup> Some of them were patients who had once been operated on and who returned because of recurrent nervousness and prominence of the eyes, often asymmetrical.

It is not generally realized that many routine cases of Graves's disease show moderate increase in exophthalmos after thyroidectomy if careful measurements are made. Indeed, most clinicians believe the reverse to be true, because this increased exophthalmos is obscured by the return of the upper eyelid to its normal position. It seems

likely that the cases of malignant exophthalmos are simply extreme examples of a mechanism that occurs generally.

If the protein bound iodine is determined in the plasma of these patients before any iodine therapy has been used, it is frequently found to be normal.<sup>24</sup> Furthermore, if iodine therapy is given to such patients in large doses, the basal metabolic rate frequently falls to definitely subnormal levels. It has been suggested, however, that thyroid therapy, alone or combined with iodine, is often the procedure of choice, for reasons already described.

These questions also bear on the general problem of hyperthyroidism, because in cases of chronic Graves's disease of more than a year's standing, there is now some question of the best mode of therapy. In many of these patients, the iodine metabolism seems to be at approximately normal levels, perhaps because the thyroid's reserve of iodine has been exhausted. Nevertheless, in patients subjected to subtotal thyroidectomy, the disease is prone to recur. For this reason, Lacey and his colleagues<sup>25</sup> have recommended a radical resection under these circumstances. The tentative opinion has also been advanced by other workers that iodine therapy in these cases may supply the raw material for a renewed outpouring of thyroid hormone in great excess. Still other clinicians fear that ultimate cardiac decompensation will take a heavy toll if nearly all cases showing even mild symptoms are not operated on. Obviously, the final word cannot be stated at present about this special group of cases. It may, however, be a useful confirmatory test to find that the plasma protein bound iodine before therapy is normal even though the apparent basal metabolic rate may be somewhat increased.<sup>24</sup> Should these cases, carefully selected, receive thyroid medication?

Another point of interest that requires further clinical experience is the use of commercial thyroid preparations in older patients with hypothyroidism and in those with frank cardiovascular disease. Meyer and Yost<sup>26</sup> have presented evidence that preparations of the whole gland may contain an unidentified material that accelerates heart action far in excess of the actual effect of the thyroid hormone itself. Indeed, they have fractionated such glandular preparations into one extract, which contains the thyroid hormone, and another, which contains the excessive cardioaccelerating material without the thyroid hormone. At present, more clinical experience is needed to determine the value of these findings, but already it seems possible that such an untoward effect may be avoided by using iodinated serum protein<sup>27</sup> in lieu of actual thyroid material.

The same thing may be said of certain purified

thyroid fractions now available commercially. In the treatment of cases subject to anginoid attacks, this point merits careful study.

\* \* \*

In summary, then, one should take advantage of the two properties of the thyroid hormone, namely, its maturing and its calorogenic effects, in rectifying disturbances in endocrine imbalance. In so doing, one must not fail to take advantage of the early years of life if growth and development are in question. In the later years of life, on the other hand, one must be careful not to outstrip the functional reserve of any organ or system in the body. It must always be remembered that all the endocrines are in league with one another, and that a change in thyroid balance alters pituitary, ovarian and adrenal function. Some of the symptoms of overdosage are usually mere nuisances, like diarrhea or oligomenorrhea. Others, such as the precipitation of heart failure or of Addisonian shock, may be rapidly fatal.

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## PROBLEMS IN THE RECOGNITION AND TREATMENT OF TESTICULAR INSUFFICIENCY\*

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MANY of the properties of the testicular hormone have long been understood by physicians from years of acquaintance with eunuchs and eunuchoids, and certain influences of the synthetic androgens were accordingly readily foreseen. Other influences of the therapeutic androgens have, however, occasioned some surprise and have prompted re-examination of testicular functions less well grasped in the past, functions that still require much work for their proper understanding. The influences of testosterone and its relatives on sexual drive and on general body metabolism are effects that may shed new light on the place of the testis in human economy.

The exact composition of the hormone or hormones secreted by the testis is unknown. Testosterone, isolated from bull testes in 1935 and large-

ly obtained at present by the degradation of cholesterol, seems to repair castration defects very well, and to possess no exceptional or unnatural properties (Koch<sup>1</sup> and Moore<sup>2</sup>). Certain active esters of testosterone, the acetate and the propionate, are now used extensively in clinical and biological work, and owe their popularity to the fact that they are four times more powerful than testosterone itself in evoking growth of the prostate and seminal vesicles of the castrate rat when subcutaneous injections in oil are given.<sup>3,4</sup> This advantage seems to lie in a slower and more favorable rate of absorption from subcutaneous oil pools in this species and does not mean that these esters approximate the natural hormone in composition. A similar and even more striking enhancement of effect is provided by implantation of testosterone in pellets under the skin.<sup>5</sup> It is difficult to say what difference it will make when the precise form of the natural androgenic secretion is

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known, but reservations derived from this ignorance should be kept in mind. Such reservations are applicable especially to the consideration of methyl testosterone, which retains much of its activity on oral administration.<sup>6</sup> It is certain that this substance does not increase urinary androgen excretion when given orally to man nearly so much as testosterone does.<sup>7,8</sup> The significance of this peculiarity is not clear, and most careful examination is desirable before the full equivalence of methyl testosterone to the testis in a clinical sense is accepted.

When testosterone or one of its active relatives is given in proper dosage to a eunuch or a eunuchoid or to a child, one of the first and most consistent and distinct reactions induced is an increase in frequency, intensity and duration of erections of the penis.<sup>9-11</sup> This response may occur within a few hours of the initial dose, usually within a few days, and may be intense enough to reach priapism. It is often accompanied by erythema and edema about the genitalia and by considerable increase in sexual desire and capacity for intercourse. As the anatomic responses to the androgens progress, this heightened genital irritability often subsides somewhat but still remains fairly distinct. This effect recedes on cessation of treatment in the majority of cases, and is not consistently simulated by responses to placebos.

It is true that the sexual activity of several lower forms of animals had long been known to be strictly dependent on testicular hormones,<sup>12</sup> but experience with man had suggested an overwhelming importance of mental attitudes for sexual drive. Although castrate men often complained of waning potency, in others both inclination and capacity for intercourse were at least to some extent retained for years.<sup>13-14</sup> It was accordingly tempting to interpret the irregular depression of sexual power after castration as psychogenic, occurring by virtue of the subject's unhappy expectations, rather than by virtue of his loss of hormones. The erotogenic property of the therapeutic androgens has, however, restored confidence in the validity of the eunuch's story of impaired sexual drive. Man in his evolutionary progress has not lost the primitive sensitiveness to erotogenic testicular secretions, but with the elaboration of cerebral function and the permeation of consciousness by sexual and quasi sexual concerns, his nervous system has grown less dependent on hormonal excitation and more dependent on the countless factors shaping emotional life. From individual to individual, the resultants of humoral and nervous or psychic forces must vary greatly. The former factor still requires attention throughout the study of the pathology of the sexual impulse.

How useful is testosterone in enhancing the sexual drive in those many men, apparently sound physically, who nevertheless suffer from sluggish sexual desire and inability to perform normal coitus? It is conceivable that the desire and potency of certain men might be increased beyond that induced by their own normal androgens sufficiently to overcome fears and misgivings that had frustrated the original normal sexual drive. The answer as thus far known is not very hopeful. Rubinstein and Kurland,<sup>15</sup> Rennie, Vest and Howard,<sup>16</sup> and Kenyon et al.<sup>17</sup> have injected testosterone propionate into normal men, and in no case has the slightest effect on frequency of erections or sexual desire been recorded. Although hypernormal excretion of urinary androgens<sup>18</sup> and nitrogen retention<sup>17</sup> can be readily induced, the sexual drive is unaffected. This is clearly no final statement; individuals vary too much for that, but it seems unlikely that the sexual drive natural to any person with sound testes can often be readily increased.

Occult testicular insufficiency, however, may exist in some impotent men. After castration of the man who has once reached sexual maturity or after discontinuance of effective androgen therapy in the hypogonad, the deep voice remains, the penis may not recede to an unmistakably hypoplastic state, genital, trunk and facial hair falls out slowly and irregularly, and considerable amounts of inactive prostatic tissue may remain palpable. It is thus quite possible that a significant reduction in the amounts of testicular secretion for fairly long periods may go undetected if observation is confined to these sluggish and unquantitative physical criteria of androgen production. It would be easy indeed to invoke psychogenesis at such times. Unfortunately, assays for urinary derivatives of the testicular hormone have not been widely applied to impotent men. Zones of overlap apparent between those with normal testes and even those who are grossly hypogonadal will probably restrict the usefulness of such procedures, however, to some extent at least. One is thus left with the therapeutic trial, easy to apply and hard to interpret. Although benefit in the treatment of impotent men with testosterone propionate has been reported, the extensive experience of Rennie, Vest and Howard<sup>16</sup> indicates that such benefit is not often secured.

Carmichael, Noonan and Kenyon<sup>19</sup> treated, with testosterone propionate, 19 men who suffered variously from inadequate sexual desire, failure to secure or sustain erections at the time of coitus, and premature ejaculation. With the exception of one man who had atrophic testes but a normal penis, prostate and secondary sex characteristics,

none suffered from pertinent organic disease. Twenty-five milligrams, intramuscularly, three times weekly was given because this seemed adequate replacement dosage in patients with gross testicular defects. Relief of the impotence was obtained in 7 of the patients—2 children were begot by these men; 11 patients were unaffected. Unfortunately, the successes do not bear close inspection. In no case was cessation of treatment or substitution of inert sesame oil for the androgen accompanied by such relapse within a few weeks as would be expected if there was genuine dependence on the testosterone propionate. At first, the patient with atrophic testes seemed to distinguish between testosterone and sesame oil, but in the end he wearied of treatment and carried on successfully for at least a month after the last injection, so that dependence was quite doubtful. The only conservative interpretation of these results is that any benefit secured was psychologic—suggestion either pure and simple or suggestion arising from an initial physiologic excitation with successful coitus and restored confidence.\*

It still remains to be seen whether testosterone propionate will cure any patient whose impotence is not amenable to rather simple inquiry, explanation and reassurance, or to treatment by placebo. My guess is that in time one will find such people—those with occult testicular insufficiency whose hormone production is below their particular nervous thresholds for adequate sexual drive. Perhaps they will be found among older men whose hormonal production is normally declining, but, in any event, they are probably a small minority of impotent men. In the search for these, however, I believe the therapeutic trial with androgens is desirable when simple psychologic methods fail. Twenty-five milligrams of testosterone propionate intramuscularly in sesame oil three times weekly, or methyl-testosterone, 50 to 100 mg., orally, daily for three weeks, should be adequate. Semen examinations at weekly intervals during such a procedure are wise. These dosages may in time reduce the number of spermatozoa and eventually cause their disappearance from the semen.<sup>21, 22</sup> Although such depression is always recovered from after androgens are stopped, so far as I know, there is no point in producing it. If such a therapeutic trial is successful, cessation of treatment or substitution of an inert substance may estab-

lish dependency on the androgen or lack of it. When treatment fails, recourse must be had to more elaborate psychotherapy.

The metabolic effects of the androgens have been of great interest to our group and, I believe, emphasize an aspect of testicular function that has received little attention. The data described here were gathered by Knowlton, Sandiford, Bryan, Koch, Lotwin and myself.<sup>16, 17, 18, 23</sup> Soon after the beginning of treatment of the eunuchoid with testosterone propionate intramuscularly, an increase in body weight is observed, amounting in our experience to 7 to 20 pounds at the maximum, and accompanied, on occasion, by slight edema of the face and ankles. The process is self-limited, a plateau appearing in forty to seventy days despite continued treatment. When the patient is examined on a constant food and fluid intake, a sharp decline in the urinary excretion of nitrogen and inorganic phosphorus, potassium, sodium and chloride is observed, while the urine volume declines and the body weight increases. During recovery from the testosterone effect, sodium and chloride, deposited largely in extracellular spaces, are quickly lost, together with associated water, while nitrogen, presumably stored as protein within cells, is still being retained. The inconspicuous losses of nitrogen for as long as thirty-eight days after cessation of therapy attest to the tenacity with which deposited protein is retained. The decline in urinary nitrogen is reflected completely in the urea fraction, and no increase in the concentration of nitrogenous constituents of the blood occurs. Fecal nitrogen is unaffected. When substantial creatinuria is induced by creatine feeding, this substance is also retained under the influence of the androgen.

The nitrogen retention has been previously described by Kochakian and Murlin<sup>24, 25</sup> in the castrate dog, and nitrogen and several electrolytes have been shown to be retained in the normal dog, as well as in an impotent man by Thorn and Engel.<sup>26</sup> In both rats<sup>27</sup> and monkeys,<sup>28</sup> creatine excretion is affected by androgens as in man. So far as work has progressed, therefore, the chemical reactions to androgens seem fairly general among animals. Exceptions in detail occur and will probably become more abundant in time as more species are studied.

The amounts of protein estimated as stored in the eunuchoid range from 109 to 395 gm. in ten to twenty-five days, far in excess of those conceivably going to the prostate and seminal vesicles. The curve of gain in body weight predicted from the protein stored, together with the associated water, falls short of the actual gain in weight and differs in its course from the actual weight

\*A possible complexity in interpreting the consequences of withdrawal of androgens should be noted, although it is well not to make too much of it at present. It may take several months for all sexual capacity to be completely extinguished in rats and rabbits when they are castrated after puberty,<sup>22</sup> and an immature drill (baboon) excited to sexual interest by androgens retained this interest for eighteen months after cessation of treatment.<sup>29</sup> Residual behavior patterns established by androgens and persisting after treatment must be considered. These may be difficult to separate from the results of suggestion in man.



curve. Retention of salt and water in extracellular spaces during treatment and their discharge thereafter probably account for the discrepancies.

It is of importance that nitrogen retention and salt and water retention have been produced in a subject with a craniopharyngioma in whom the anterior lobe of the pituitary body was reduced to a mere shred at autopsy.<sup>20</sup> It is therefore unlikely that these effects are mediated through the pituitary body.

The basal metabolic rate is increased by moderate dosages of testosterone propionate<sup>10 21</sup> In the extreme form of this effect, heat production may rise to levels as high as +40 per cent when large doses of methyl testosterone are used, as in the experiments of McCullagh and his co workers<sup>20</sup> The elevation is much less striking when amounts of testosterone propionate conceived as replacing the testes are given<sup>18</sup>

The retention of sodium, chloride and water is analogous to that produced by the chemically related adrenocortical substances in men and dogs with intact adrenal glands, an analogy well supported by the observations of Thorn and Harrop,<sup>30</sup> and Thorn and Engel<sup>20</sup> on the salt retaining properties of several sex hormones The analogy is incomplete, however, because the urinary excretion of potassium is characteristically increased by adrenal substances rather than reduced, as with testosterone propionate This partial imitation of one steroid by another is no new phenomenon Many other interesting examples could be cited

The retention of nitrogen, creatine, inorganic phosphorus and potassium suggests a somatotropic effect of testosterone propionate Papanicolaou and Falk<sup>31</sup> observed that testosterone propionate produced hypertrophy of the temporal muscles of the castrate male guinea pig and of the castrate or normal female There was also an increase in total muscle mass It is likely that new protein is deposited in muscle of man and probably elsewhere as well Attempts are now being made to record the strength and fatigability of the muscles of hypogonadal men after treatment with androgens, and the results are thus far encouraging.<sup>32 33</sup>

Recent evidence of great value demonstrates that, in certain boys, administration of androgens induces distinct gains in height Webster and Hoskins<sup>31</sup> found 8 hypogonadal boys to grow on the average of 1.36 cm. per hundred days before treatment with testosterone propionate, 3.6 cm. during treatment, and 1.56 cm. after treatment Browne and Ross<sup>33</sup> and McCullagh<sup>40</sup> added data of this same type, and Albright and his associates<sup>37</sup> secured increases in height in dwarfs with convincing physiologic evidence of anterior pituitary de-

fect Dorff,<sup>38</sup> using an identical twin as a control, secured an excellent demonstration of increased somatic growth in a short, poorly developed boy with chorionic gonadotropins, which stimulated androgen production by the boy's own testes It is of interest that early epiphyseal closure has not as yet been induced in such subjects From experience with older eunuchoids, however, and from the notorious early closure of epiphyses in children with precocious puberty, I should expect that carelessly large and protracted treatment of the young boy with androgens would in time effect epiphyseal fusion

The responsibility of the testicular hormone itself for the normal adolescent growth spurt thus becomes clear, and the reason for the association of precocious genital and somatic development in boys with testicular tumors is now, I think, apparent It is best, however, that such powerful properties of the androgens as these should be utilized by the physician in the young only when it is established beyond doubt that the patient's own testes will not spontaneously assert themselves. Under such circumstances, attempts at stimulation with chorionic gonadotropins are, I believe, the first choice Androgens may be used in event of failure

Two important therapeutic applications of the somatotropic properties of the androgens have been made recently by the group at the Massachusetts General Hospital, Albright, Parson and Bloomberg<sup>33</sup> have proved that testosterone propionate will induce immediate nitrogen and phosphorus retention and eventually calcium retention in those with Cushing's syndrome, and they have observed that these anabolic influences were accompanied by an improved sense of well being and physical efficiency They conceive these effects as counteracting protein wastage inherent in the disease Although further chemical support for the concept of protein loss as a critical metabolic event in Cushing's syndrome is admittedly necessary, guarded use of the androgens is desirable on the basis of this experience The risks of further depressing testicular function in the male, and of protracting the amenorrhea and of advancing the masculinization of hair, voice and clitoris in the female must be carefully assessed, and dosages sought that will, if possible, avoid them. Profound debility seems to be the essential indication for therapy, and the defect likeliest to be remedied There is no reason to believe that hypertension is affected by androgens

The metabolic responses to androgens in those with hypopituitarism are in time accompanied by significant gains in physical efficiency, according

to Albright et al.<sup>37</sup> Thus, the role of the testis in the metabolic consequences of pituitary defect requires examination. Careful use of the androgens, with due consideration of their possible disadvantages, will define the value of this tool in pituitary failure.

Unpublished work of our own indicates that testosterone propionate exerts at least most of its characteristic metabolic influences in the aged man. How important this is from the functional standpoint is unsettled.

Thus, one begins to think of the nongenital properties of the androgens and to seek means of gauging their value in testicular insufficiency and in other pertinent disease. The work is young and the future unsettled, but the prospects of making something interesting and useful out of the somatotropic effects of these compounds are not too bad.

#### SUMMARY AND CONCLUSIONS

The testis is of importance in initiating and maintaining the sexual drive and the capacity for intercourse in the human male, although this role is shared by nervous factors.

Testosterone and its active relatives, which are known to enhance sexual excitability in the hypogonad, have not as yet been shown to affect men with sound testes.

Occult testicular insufficiency, however, may play a role in causing impotence in men without obvious testicular defect. At present, however, it seems likely that such testicular responsibility is rare.

Testosterone propionate relieves perhaps a third of impotent men, but discontinuance of treatment or substitution of placebos is not followed by prompt relapses, so that true dependence on androgens is difficult to establish. Conservative interpretation necessitates regarding the benefit as due to suggestion. In the search for cases of true occult testicular insufficiency, brief therapeutic trials with testosterone and its relatives, critically examined, are worth while.

Testosterone propionate induces retention of nitrogen, creatine, inorganic phosphorus, sodium, potassium and chloride and causes an increase in body weight and in the basal metabolic rate of underdeveloped men. Growth in height of undergrown, underdeveloped boys has been established. It is suggested that certain of these effects at least occur independent of the anterior pituitary body. The reasons for the association of sexual development with enhanced somatic growth during normal adolescence and in precocious puberty are hence clearer.

These somatotropic properties of the androgens may be of benefit in the treatment of certain aspects of pituitary insufficiency and Cushing's syndrome. There is need for further exploration of these possibilities.

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## THE USE OF FEMALE SEX HORMONES IN DISORDERS OF WOMEN\*

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### FUNCTIONAL DISORDERS

THE application of the term 'functional' to any disorder means that known pathologic causes have been ruled out, that the real cause is unknown, and that the disorder may not be permanent. This word reflects the still unsatisfactory state of knowledge concerning those disabilities in women that are attributed to hormonal imbalance or lack, and indicates that any treatment must, for the present, be largely empirical. It also implies that all measures conducive to better general health, such as proper diet and elimination, emotional adjustment, regulation of habits, treatment of infected foci and anemia, and thyroid therapy, should be instituted, if necessary.

#### Amenorrhea

In patients with functional amenorrhea, whether primary or secondary, the really important aim is to produce ovulation. The available gonad stimulating extracts of anterior hypophyses or of pregnant mares' serum have been tried with only rare success because, perhaps, they are not potent enough or, more probably, because they stimulate antihormonal bodies, containing as they do for eign protein, or because the primary disturbance is not gonad stimulating insufficiency. Women with functional amenorrhea do not usually give the impression of having a pituitary disturbance. They either appear perfectly normal or are like her to show stigmas that one associates with adrenal hyperactivity. Evidence is appearing that more and more interrelates the adrenocortical and ovarian hormones. Analysis of this relation may give a clue to the cause and cure of functional amenorrhea.

The induction of simple anovulatory uterine bleeding is sometimes desirable for psychiatric reasons and may be accomplished by trials with the preparations mentioned above or with placental

hormone, chorionic gonadotropin or the steroid hormones, estrogen and progesterone.

#### Dysmenorrhea

Whether or not any endocrine imbalance exists in patients with essential or primary—that is, functional—dysmenorrhea remains to be demonstrated. What has been shown is that the symptoms may be mitigated or prevented by various hormones, provided they are given at such times during the cycle and in such amounts as to change the endocrine balance. The most dependable of these methods appears to be that of Sturgis and Albright,<sup>1</sup> who, by injecting estrogenic substance beginning on the sixth day after the start of menstruation, prevent ovulation and luteinization, thereby preventing the dysmenorrhea. This method is completely effective only during alternate months, but after a series of treatments, the intervening periods are likely to become less painful. At present, the cost to the physician of the estrogenic hormone for each painless catamenia induced is about \$13.00. Because most physicians hesitate to upset a physiologic process, even to alleviate an exaggeration of the usual response to it, and because of the high cost of hormones, they tend to temporize by means of general health measures and simple antispasmodics and analgesics, especially with girls, until the passage of time or pregnancy brings amelioration. In spite of a trial of all nonoperative measures, an occasional case of functional dysmenorrhea must be submitted to presacral neurectomy, an essentially curative procedure without known consequent disability, if well executed, although it is radical and apparently unphysiologic.

#### Premenstrual Distress

Another functional disorder, so-called "premenstrual distress or tension," includes any or all the following symptoms: premenstrual headache, often simulating migraine, depression, irritability, epigastric distress, nausea, sense of abdominal swelling and sore breasts. These symptoms

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are common, especially in women between the age of thirty-five and the menopause. Because they are accompanied by premenstrual increases of weight and occasionally by local or generalized edema, they are thought to originate from sodium and water retention associated with changes in sex-hormone metabolism. A simple treatment introduced by Greenhill and Freed,<sup>2</sup> consisting in sodium chloride restriction and ammonium chloride ingestion during the last two weeks of the cycle, is reported to give gratifying relief. This method is presumably treating the result and not the cause of the disturbance. Satisfactory relief may also be obtained by the administration of sufficient estrogen or progesterone in the second half of the cycle, or by giving fairly large amounts of oral estrogen daily throughout the cycle. This is perhaps a more physiologic treatment, since these patients are thought to have beginning ovarian failure, and such therapy is likelier to relieve the breast symptoms.

#### *Uterine Bleeding*

Functional uterine bleeding is usually no therapeutic problem in women over forty years of age, since radiation castration is so simple and dependable, although it is neither ideal nor wholly desirable. Complete examination under anesthesia is a necessity in these patients, because it is the only way of making reasonably certain that cancer is not present. In younger women who are obviously not going to have a remission to normal cycles, either spontaneously or from general constitutional treatment with emphasis on the administration of thyroid and iron, it seems wiser to try curettage and then hormones before resorting to more radical surgery or temporary inhibition of the ovaries by radiation, especially since there can be no positive assurance that either of these procedures will be permanently curative in any patient, unless performed radically enough to involve the possibility of permanent damage. Chorionic gonadotropin, when injected during the flow in daily doses of 1000 to 2500 international units for four to eight days, may be expected to stop functional uterine bleeding at least temporarily in about 75 per cent of cases and to result in apparent cure in about 40 per cent. If it is to be effective, chorionic gonadotropin must be given in large doses, for smaller amounts may aggravate the bleeding. Unfortunately, large injections may be painful. Equine gonad-stimulating hormone has not yet been found to be of dependable value in this condition. Testosterone in large daily dosage, although it is costly, stops functional uterine bleeding, apparently through the desirable effect of temporary ovarian inhibition. Progesterone ap-

pears to be the ideal drug, at least for inhibiting bleeding in a physiologic manner, even if it may not remedy the basic cause, but thus far it has been too expensive for extensive clinical studies.

#### *Habitual Abortion*

Although habitual or threatened abortion or threatened miscarriage involves various and complex possible causes, the known necessity of adequate progesterone for normal gestation indicates its use in these precarious states. Circumstantial evidence implies that much more progesterone is secreted than appears as urinary pregnandiol. Hence, I believe it might be of more value than reports at present suggest if it is given in much larger doses. Furthermore, I believe it would be more clearly valuable if injected with estrogen.

In experimental work, estrogen is necessary for the optimum effect of progesterone and for stimulating and maintaining luteal activity. That it is also necessary for progesterone activity in human beings is indicated by the fact that its increases and decreases precede or accompany increases and decreases of progesterone both in menstrual cycles and in pregnancy, including those cases of threatened abortion in which changes in these hormones have been detected. Evidence of progesterone secretion is never found in the absence of estrogen. Conversely, secretion of estrogen without consequent or concomitant secretion of progesterone does occur and may result in typical functional uterine bleeding. In fact, all the available evidence shows that these two hormones are complementary, that they enhance and regulate each other's properties, and that they are physiologic companions. The idea that estrogen may cause abortion in human beings may be completely disregarded, since otherwise we should all certainly by now be acquainted with such use.

These considerations make me optimistic that better results will be achieved in all conditions in which estrogen or progesterone alone has already seemed of value just as soon as one becomes accustomed to the idea of administering these hormones in combination and their cost drops to a practical range.

#### *Sterility*

Functional sterility involves so many factors in each partner that no straightforward indication for the use of hormones has been determined. Poor semen and failure of ovulation continue to complicate trials of gonad-stimulating factors, but general constitutional measures and postcoital insufflation during the time of possible ovulation should not be disregarded. The oral administration of estrogenic

substance in moderate amounts for months has often seemed worth while

#### OTHER DISORDERS

##### *Senile Vaginitis*

Senile vaginitis severe enough to be symptomatically disturbing is a relatively rare condition, and usually responds to simple antiseptic measures and persistent cleanliness. The characteristic slight staining demands thorough investigation. To hasten cure both by its local effect in increasing acidity and stimulating activity of vaginal epithelium and by its general beneficial effect in the menopause, estrogen is helpful if given in large dosage. I think that a combination of estrogen and progesterone will in time be found even better.

##### *Vulval Itching and Irritation*

Itching and irritation of the vulva, especially with involvement of the perineum, the perianal region, the intergluteal fold and the upper inner thighs, suggest urinary sugar and the vaginal trichomonal or fungous infection as causes. Cleanliness and a fair trial of a mild sulfur and salicylic acid ointment are likely to give prompt relief if a fungus is the cause. If, however, the vulva alone itches and is whitened, thickened and crinkly, more deep seated and irreversible pathologic changes are present. Although there is as yet no evidence to justify a fear that the use of hormones may cause cancer in human beings, in this site or elsewhere, prolonged intunctions with estrogen in tissues of known potential malignancy do not seem

warranted and, being only palliative, delay the relief that attends the simple operation of complete superficial vulvectomy.

##### *Cystic Disease of the Mammary Glands*

The background of cystic disease of the mammary glands and its end stage is so uncertain that no place for any hormone in treatment is apparent.

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The practical use of female sex hormones in disorders of women is indeed still limited. Clinical trials are vastly easier than fundamental investigation, but until more basic knowledge is acquired, voluminous contradictory and poorly controlled results will continue to appear and bewilder even those who are supposed to have more than average familiarity with the field. Many physicians believe that they are behind the times in the matter of hormone treatment and that others can accomplish more with hormones than they can. From my own experience, in practice and laboratory and from a fairly intimate acquaintance with the literature, I can assure them that they are not really behind the times, for just as soon as a treatment is found to be clearly and consistently effective, it rapidly comes into universally accepted use. Only estrogen, alone, in the treatment of the menopause has reached that goal.

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## THE CURRENT STATUS OF FEMALE SEX HORMONES\*

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A DECADE ago, endocrinologists were confident that within a few years the new knowledge that they had secured would come into productive use to solve many of the problems of gynecology. Toward the end of that decade, an eminent gynecologist, who had himself contributed a great deal to the newer developments, stated in effect that, except for a certain amount of amelioration of the discomforts of the menopause, gynecic endocrinology had contributed practically nothing to the welfare of women. The condemnation was no doubt too sweeping, but it serves to raise the question why the discoveries of the investigators have failed to yield more substantial clinical returns. It is the chief purpose of this paper to reconsider some of the fundamental evidence for the light that may be shed on this problem. A second purpose is to suggest certain possibilities for the extension of clinical research, with the idea of making the physiologic discoveries more fruitful.

## PHYSIOLOGY

Among the many important discoveries regarding the sexual physiology of women, one of the most meaningful is that destruction of the anterior lobe of the pituitary gland leads to a profound depression of the reproductive structures and functions. The further discovery that the sex depression can be corrected by the use of pituitary grafts or extracts shows that it is due to the loss of one or more stimulating hormones. By chemical manipulation of the extracts, the stimulating material has been obtained in high concentration and shown to be of protein nature. It is known as gonadotropin. More recently, gonadotropin has been separated into two chemical fractions, pure or nearly pure, one of which stimulates the corpus luteum and one the follicular apparatus. These fractions are LH (luteinizing hormone) and FSH (follicle-stimulating hormone). The fundamental controlling influence of the anterior lobe of the pituitary gland on the ovaries is now firmly established. This key fact must be kept in mind in practical research on the sex functions.

But the ovaries—including the corpora lutea—also exercise a large measure of control over the pituitary gland. This arrangement leads to a com-

plex set of interrelations that should also be taken into account in attempting to apply physiologic knowledge to problems of reproductive dysfunction.

The best known feature of ovarian physiology, as such, is the secretion of the estrogenic hormone. This is formed chiefly by the follicular apparatus. The secretion reaches full tide at the midmenstrual period when the follicle is ready to discharge an ovum. It is at this time that the phenomenon of heat occurs in animals and that concern with heterosexual matters is at its height in women. As the estrogen output has been increasing, it has been exercising a cumulative inhibitory effect on the anterior lobe of the pituitary gland, so that when estrogen is at flood tide, FSH is at ebb. The ovary is thus deprived of its pituitary support, and estrogen secretion, in its turn, largely ceases. Then, after a lag, the brakes are released, that is, the inhibition of the pituitary gland wears off, the secretion of FSH begins again, causing the secretion of more estrogen, and the total cycle is repeated. Thus, the ebb and flow of gonadotropin bring about an ebb and flow of estrogen, and vice versa.

The actual drive behind both sets of cyclic events is, of course, the secretion tendency of the individual cells, but the factor that makes for cyclicism is largely the lag in the influence of each of the hormones on its target organ. There is some evidence, however, that the cyclicism resides more in the pituitary gland than in the ovary—the evidence being chiefly that spayed monkeys, under the constant influence of estrogen supplied at a minimal effective rate, can sometimes be made to menstruate regularly.

But this relation of FSH to estrogen is only half the story. The trend of recent evidence is to show with increasing clarity that a similar relation exists between the luteinizing hormone and the corpus luteum. Although explicit quantitative data are yet lacking, the end results indicate that, while the FSH tide is receding, the LH tide is rising and thus ensuring the development of a new corpus luteum. This structure begins at once to secrete progesterin. After a few days, the progesterin level reaches a point at which the production of LH by the pituitary gland is halted, and progesterin formation then wanes. Thus, a second reciprocal series of cyclic events is set up. These alternate in phase with the FSH and

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estrogen cycles. The total result is like that of two seesaws operating side by side so that while the end of one is going up the corresponding end of the other is going down.

The consequence of this double reciprocating arrangement is that on every day of the month the four hormones concerned—LH, progesterin, FSH and estrogen—are normally present in different absolute amounts, as well as in different proportions of one to another. It is only by this nice and constantly shifting system of checks and balances that the normal menstrual cycle is maintained. Any serious dislocation of the fourfold balance spells menstrual disorder.

#### PRACTICAL AND THEORETICAL APPLICATIONS

Although a certain amount of palliation of menstrual disorders can sometimes be achieved without taking these fundamental facts fully into account, actual restoration to normality, which is of course the real goal of the therapist, cannot be obtained.

First, there is an important consequence of the fact that the gonadotropins are protein substances: if given at all, they must be administered in such a way as to escape digestion. This fact places a considerable limitation on their practical use. Secondly, the gonadotropins, LH and FSH come into action alternately, and if Nature is to be imitated at all closely in the control of cyclic dysfunctions, they must therefore be given in sequence, with due consideration of the proportion of the cycle in which each is dominant. If both the gonadotropins are given together, they must necessarily be largely self-defeating remedies: what is gained by the promotion of estrogen secretion in phase is lost by the promotion of progesterin secretion out of phase, and vice versa. But at the present time, only mixtures of the two pituitary gonadotropins are available. Thus, an impasse is reached, and at a stroke, half the theoretical possibilities of ovarian control are lost. The practical conclusion of the matter is that pituitary gonadotropins as at present available are probably not worth using.

However, according to current findings in Cohn's<sup>1</sup> laboratory, the pituitary FSH is an albumin whereas LH is a globulin; hence, they could perhaps be prepared separately in commercial practice without too great difficulty. However, another difficulty is inescapable: the yield is very small, and these two hormones are consequently too expensive for the use of anyone but investigators and millionaires.

Less expensive than the pituitary hormones are the various chorionic gonadotropins that are ob-

tainable from human placentas and pregnancy urine. These, however, have the physiologic function of promoting the relatively steady state of pregnancy and not the cyclic events that are principally concerned in this discussion. Whether these products could be chemically manipulated to give fractions having purely follicle-stimulating and corpus-luteum-stimulating properties remains to be determined. The mare-serum gonadotropin was formerly believed to give pure follicle stimulation, but more recent work shows that it also influences corpus-luteum development. In recapitulation, then, the successful therapeutic control of cyclic ovarian functions in large measure still awaits the production of separate follicle-stimulating and corpus-luteum-stimulating hormones.

Even when such preparations become available, however, another practical difficulty will still remain. In the natural scheme of things, the gonadotropins flow into the blood stream, not at a constant rate, but with everchanging ebb and flow. Therefore, the therapeutic mimic, if he is to conform to Nature, must change the dosage every day in the month, and at some stages of the cycle he must give both hormones together.

A partial escape from the manifold difficulties of gonadotropin therapy lies in efforts to control the secretion of these substances by the patient herself. The therapist may elect to give the ovarian hormones, estrogen and progesterin, instead of the gonadotropins, and may depend on their influence on the regulator gland to maintain the ebb and flow of the gonadotropins. The same considerations regarding sequence and shifting dosages apply, of course, to the ovarian hormones as to the gonadotropins.

Is this all so complex as to add up to therapeutic nonsense? It should be noted that the complexities are Nature's doing and not the endocrinologist's. The facts can only be faced. Unless physiologic conditions can be restored in the ailing woman, she must necessarily remain in a pathologic status. It is true that any one of the four hormones can be given arbitrarily in any dosage desired and, so given, may by good luck restore normality on some day of the cycle, but by the same token must necessarily induce abnormality during the other twenty-seven days. The best, therefore, that can be hoped for by any system of constant dosage is the substitution of one abnormal condition for another. It may or may not be better than the abnormality that it supersedes. As a matter of clinical fact, it is sometimes better, and the patient secures considerable relief. To determine just how much clinical results could be

improved by following a stair-step pattern of dosage levels of the sex hormones and using them in normal temporal sequence, more research is needed.

Not only the slopes of the sex-hormone production curves but also the quantitative levels at which the curves are set are important characteristics. Estrogen, for example, is both a stimulating and a depressing agent, the end effect depending largely on the amount that is used. In the lower dosage range, it stimulates the uterus and various other secondary reproductive structures. It also supports the corpus luteum and facilitates the metabolism of its hormone, progesterin. There is some evidence that it may also stimulate the anterior pituitary gland and the ovary itself. But as the blood-estrogen level increases, the effect shifts predominantly to depression, and especially depression of FSH production. Through this depressive range, estrogen when given as a sex stimulant is largely a self-defeating remedy. By analogy, it is as though the motor of a car were supplied with more gasoline but with the brakes simultaneously tightened. The car under such conditions may actually be brought to a standstill. Finally, by increasing the dosage still further, the braking effect can largely be overcome and stimulation of most of the target organs secured. To return to the analogy, the car can be forced to go ahead even with the brakes set, but that procedure is not good for the car. Likewise, a woman with a vital part of her anterior pituitary gland paralyzed is certainly not in a good physiologic condition. The best that can be hoped for with unphysiologic dosages is some sort of passably good performance in a fundamentally maladjusted organism.

It is possible that further research will show that, in a substantial proportion of clinical cases, when stimulation is desired, more could be accomplished with estrogen by keeping the dosage within the primary stimulating range and giving it time gradually to exert its influence than by administering the abnormally large doses that are commonly employed when stimulation is desired.

In the use of the gonadotropins and primary sex hormones, various difficult problems of diagnosis are, of course, involved. In any type of replacement therapy, it is essential to know just what is to be replaced and just how extensive is the deficit that is to be corrected. However, an adequate consideration of these problems is impossible here. It may only be reiterated that menstrual disorders may be due to either pituitary or ovarian misbehavior. Better results would presumably be obtained with gonadotropins in the

one event and with primary sex hormones in the other—provided, of course, that these are given in appropriate dosage and sequence.

So far as I know, there is only one clinical situation in which current therapeutic practice compares at all adequately with physiologic principles. That is in the treatment of the menopause. This is a time of transition in which the waning production of ovarian hormones takes the brakes off the anterior pituitary gland and allows the body to be flooded with gonadotropins. The exuberance can be checked in any one of several ways and, according to present evidence, with about equal success. X-ray treatments can be directed at the pituitary gland, or primary sex hormones in depressing dosages can be given. Estrogens or androgens are about equally effective, except that if the dosage of androgen is too high the woman may grow a mustache or show other evidence of masculinization. There seems to be, however, a fairly wide margin of safety.

Another striking fact, which the practical therapist conventionally ignores, is that women produce nearly as much male sex hormone as men. The estrogens and androgens apparently circulate in fairly definite proportions, one to the other. Just what Nature is about in setting up this curiously paradoxical state of affairs remains, so far as I know, a complete mystery. But it seems to be necessarily a fact that whenever estrogen is administered in significant dosage the normal estrogen-androgen ratio is disturbed. It is possible that the arrangement is meaningful and that the therapist may have to reckon with that meaning before his results become entirely satisfying either to himself or to his patients. As an empirical procedure, it might be worth while to study the comparative effects of estrogen given by itself and also given with balancing doses of androgen—both being kept within physiologic limits of quantity.

Another theoretical, if not practical, complication in gynecic endocrinology is that the adrenal cortex is able to produce sex hormones, both estrogens and androgens. This potentiality is most easily recognized when cortical neoplasm or hyperplasia results in the masculinizing of women or the feminizing of men. Sex hormones are often found in unusual amount or type in the urine of such patients. What part the adrenal glands may play in cyclical sex activities of normal women is, so far as I am informed, completely unknown. It is possible that a significant relation exists, and it may be one of practical moment; this is, of course, a proper subject for research.

An additional hormone that has considerable



influence on the reproductive processes is prolactin. It, too, is an anterior pituitary derivative. Although prolactin has been discussed mostly in relation to mammary gland activity, it has an essential relation with the sex glands proper. As Riddle<sup>2</sup> showed early in the course of his studies, this hormone has a rather marked depressing effect on both the ovaries and the testes. In rodents, at least, it also has a remarkable effect on the instinctual drives, arousing strongly the maternal impulses. By its use, a virgin rat can be made to adopt and mother not only baby rats but also mice, rabbits or even squabs. Nature apparently makes some little use of prolactin as an agent for depressing the ovaries of women, thus producing amenorrhea during the early weeks of nursing. Whether aberrations of prolactin secretion play any significant role in the ordinary menstrual disorders is, I believe, quite unknown. Further research might reveal practical aspects of that possibility. What therapeutic use prolactin might have further in the prevention of pregnancy or in the assuagement of overaridant amatory proclivities in women also seems to be an appropriate matter for clinical investigation.

The purpose of this discussion has been chiefly to suggest some of the possibilities of research that might improve the yield of practical clinical results. The fundamental physiology is complex; the application of that physiology in clinical practice will probably have to be equally complex to give the best results. Particularly, stair step dosage and proper timing of alternating materials will perhaps prove to be absolutely necessary conditions to success in many cases. Except for the treatment of menopausal disturbances, there appears to be little hope in the traditional patterns of drug therapy. There is not now and probably never will be any effective easy way to practice gynecology by using endocrine therapy.

#### SUMMARY AND CONCLUSIONS

Some of the older and the newer physiologic evidence is re-examined in relation to potential clinical applicability. The normal cyclic sex behavior of women is the result of several complexly interacting controlling factors. Serious derangement of any one factor can lead to clinical dysfunction. The goal of the therapist is to restore normality by substituting physiologic for pathologic ovarian behavior. To accomplish this, the factor or factors at fault must be recognized and appropriately dealt with.

The fault may lie in the anterior pituitary gland. Any one or more of three hormones may be involved—two gonadotropic factors (FSH and

LH) and prolactin. These are protein bodies and must therefore be administered parenterally. They are expensive. The first two should be administered in proper alternating sequences. At present, only mixtures are available; hence gonadotropic therapy is theoretically self-defeating. Pregnant mare preparations give purer but not entirely specific effects. Prolactin serves under normal conditions as a gonad depressant; research may show it to have some clinical value aside from its stimulating effect on the mammary glands.

More practicable for substitution therapy are the sex hormones proper, the estrogens and progesterone or their synthetic substitutes. These, too, must be given alternately and in phase, if their natural production is to be imitated. Each depresses the production of its corresponding gonadotropin.

All four of the gonadotropic and primary sex hormones are secreted at daily varying rates so that the blood titers, as well as the proportions existing naturally among them, differ on each day of the month. Restoration of normality therefore necessitates stair step dosages, in addition to sequential administration.

The estrogens have a three phase influence, depending on dosage. In the smallest effective range, pure stimulation seems to result. In the intermediate range, the anterior lobe of the pituitary gland and the gonads are depressed, so that the total effect may be depression. In the highest ranges, the depressions may be overcompensated. This is the conventional but pathologic range that is commonly employed. Such overdosage is theoretically indicated only in treatment of the menopause.

The adrenal cortex is capable of forming several sex hormones. More research is needed to determine whether they play a role in the normal sex activities of women and thus enter into the therapeutic equation.

Women secrete both male and female sex hormones in somewhat constant proportions. Research is needed to determine whether the male hormone plays a physiologic role and what its therapeutic value in conditions other than the menopause may be.

It is emphasized that the normal physiologic mechanisms are in part not yet known and that Nature's use of the sex hormones, even as now known, is but poorly imitated by the practical therapist.

25 Shattuck Street

#### REFERENCES

1. Freydell H. L., Lee M., Hsaw F. I., and Coyle E. I. Studies in the physical chemistry of the anterior pituitary hormones. *Endocrinology* 26:79 1934-1940.
2. L. H. R. I. L. and Riddle O. Temporary suppression of estrous cycles in the rat by prolactin. *Proc. Soc. Exper. Biol. Med.* 34:1 1933-1936.

seconded by Dr. Fitz, and it was so ordered by vote of the Council.

### *Study of the Practice of Medicine by Unregistered Persons*

The chairman, Dr. Richard Dutton, Middlesex East, reported that the committee had nothing to report. It was moved by Dr. Lund and seconded by Dr. Fitz that this report be accepted, and it was so ordered by vote of the Council.

### *Committee to Meet With Massachusetts Hospital Association*

There was no response from the chairman, Dr. Howard M. Clute, Suffolk.

### *Medical Preparedness*

Dr. Fitz reported that his committee had nothing to report. It was moved and seconded that the report be accepted, and it was so ordered by vote of the Council.

### *Committee to Examine WPA Records*

Dr. Guy L. Richardson, Essex North, before offering his formal report (Appendix No. 10), spoke of a physician who complained to his Senator that he was not getting enough WPA work. Dr. Richardson said that this situation was bad, and added that the physician in question had been advised to send in the full matter of his complaint, whereupon the matter was dropped.

Dr. Richardson spoke of hernias which developed in WPA workers and said that, except in emergency, it was the ruling of the WPA authority that, if these hernias were to be operated on, the operation would have to be performed in the Marine Hospital.

Dr. Richardson moved the acceptance of the report. Dr. Conley seconded the motion.

Dr. William E. Browne, Suffolk, said that the WPA officials were generally very fair. He said, however, that this particular ruling might be very hard on the person who developed a hernia in North Adams and had to go to Brighton to have it repaired. Dr. Bearse was also critical of this ruling. Dr. Richardson said that his committee had protested the ruling, which had come from the Commission in Washington, because of the unfavorable experience which it had in these cases when the ruling was otherwise. Dr. Peirce H. Leavitt, Plymouth, said that it was an unfair ruling and that he hoped the committee would continue to try to have it changed.

There was further discussion by Drs. Bagnall, Richardson and Browne. The question was demanded from several sources in the Council. Dr. Ober put the motion, and it was passed.

### *Maternal Welfare*

There was no response from the chairman, Dr. Judson A. Smith.

### *Study of Practice of Medicine*

Dr. Dwight O'Hara, Middlesex South, read the report (Appendix No. 11) and moved its adoption. This was seconded by Dr. Hornor.

Dr. Mongan asked what was the present status of the law in regard to the standards of medical education in Massachusetts. Dr. O'Hara said that it was his understanding that the matter was in the hands of the Approving Authority, which is empowered to act in 1945.

Dr. Mongan said he did not understand it that way. He spoke of the several extensions of the date when this law would become operative which had been granted by the Legislature. He said that this last extension ended in 1940.

The Secretary relayed a conversation which he had had with the secretary of the State Board of Registration in Medicine, in which the latter said that the schools had until 1945 to live up to whatever regulations the Approving Authority made. He further said that the secretary of the State Board of Registration in Medicine had promised to send to him certain information about the activities of the Approving Authority and that that communication was awaited.

Dr. Mongan spoke of the theory under which these extensions were granted and said in substance that the first extension was granted so as not to penalize any student who had in good faith entered a school whose standards might possibly be questioned. He moved, "That the President and Secretary take upon themselves to inquire from the Attorney General's office what, in the opinion of the Attorney General, is the interpretation of the law."

Dr. Ober announced that there was a motion before the house and that if Dr. Mongan's thought prevailed it would have to be offered as an amendment to the original motion. The Secretary said that it was his belief that the Attorney General would not give an opinion on a matter of law to a private organization such as the Society. These opinions are usually reserved for departments which are in the government. Dr. Mongan thought this might be so.

Dr. Norman A. Welch, Norfolk, said, and he asked Dr. O'Hara to correct him if he was wrong, that it was his understanding of the law that it is now effective for the scrutinizing of the education of students who entered these schools in September, 1941, and that these schools are to be under this scrutiny during the next four years, to deter-

mine the education which they give the entering classes that go in this year Dr O'Hara said that this was his understanding

The motion to accept the report was put by Dr Ober and was passed

Dr Mongan moved that the matter in question be given the attention of the President and Secretary with a view of enlightening the Council concerning what the situation is This motion was seconded by Dr Fitz and adopted on vote of the Council

#### APPOINTMENTS

Dr Ober said that in making the following appointments he had had the assistance of the Executive Committee He added that by this means he hoped to make better appointments than otherwise would be possible

Dr LeRoy A Schall, Middlesex South — chairman Auditing Committee

Dr John Rock, Norfolk — member Auditing Committee

Dr Reginald Fitz, Suffolk — chairman Committee on Postgraduate Instruction

Dr James C McCann Worcester — chairman Special Committee Concerned with Prepaid Medical Care Costs Insurance

Dr Elmer S Bagnall, Essex North, and Dr Peirce H Leavitt, Plymouth — members, Special Committee Concerned with Prepaid Medical Care Costs Insurance

Dr Daniel L Lynch Norfolk — member Committee on Industrial Health

Dr Walter G Phippen Essex South — consultant to the Joint Committee on Health Education of the State of Massachusetts

Representatives from the Massachusetts Medical Society to the Massachusetts Central Health Council

Dr Robert J Carpenter, Berkshire

Dr Francis P Denny, Norfolk

Dr George D Henderson, Hampden

Dr William D Kinney, Barnstable

Dr Erwin C Miller, Worcester

Dr Robert B Osgood, Suffolk

Dr Eugene W Beauchamp and Dr Stanley C Cox — councilors, Hampden

Dr John M Murphy — councilor, Hampshire

Dr William J Brickley and Dr Maurice Fremont Smith — councilors, Suffolk

Dr Frederic Hagler — supervising censor Hampden

Dr James B Bigelow — censor, Hampden

Dr Henry A Robinson and Dr Daniel J Inley — censors Norfolk South

It was moved, seconded and passed that the Secretary be instructed to cast one ballot confirm

ing these appointments The Secretary announced that this direction had been complied with

#### OTHER BUSINESS

Dr Ober then announced that the meeting was now open for any business that might legally come before it

The treasurer, Dr Butler, asked the Council for a special appropriation of \$125.00 to cover the expenses of the Executive Committee He offered this as a motion It was seconded by Dr Mongan and adopted by vote of the Council

There was much discussion about certain additions to the Committee on Public Relations Dr Bagnall moved that the vice president, president elect and secretary be added to the committee, that the president elect be authorized to serve as vice-chairman of the committee and that all three additional members be without authority to vote This motion was seconded and adopted on vote of the Council

Dr J Harper Blaisdell, Middlesex East, moved that the President appoint a committee of five, which shall consider necessary and desirable changes in the by laws and which shall report its recommendations in writing at the next meeting of the Council Dr Blaisdell said that the by laws need many changes He pointed to the section which provides for the election of a president elect and stated that, as this reads, the president elect serves for one day only He gave Dr Dutton credit for the initiative in this matter Dr Fitz seconded Dr Blaisdell's motion, and it was so ordered by vote of the Council

Dr MacLachlan discussed House Bill 460, and under the authority of the Middlesex East District Medical Society (September 17, 1941) offered the following motion

That the Committee on State and National Legislation be instructed to take any and all such action possible to modify amend and/or clarify the provisions of the Premarital Examination Law (House Bill 460)

It was seconded by a councilor Dr MacLachlan said that there were a great many members of the Society who do not like this law He added that apparently it had been approved by the Committee on State and National Legislation, although he was sure that the Society did not know of its approval He then proceeded to read from the law The motion was passed

There being no further business before the Council adjournment was ordered at 3:15 p m

MICHAEL A TIERIE, Secretary

## APPENDIX NO. 1

## ATTENDANCE

BARNSTABLE	Richard Dutton	H. J. Inglis	C. C. Lund
W. D. Kinney	K. L. MacLachlan	I. R. Jankelson	H. C. Marble
BERKSHIRE	R. W. Sheehy	C. J. Kickham	G. R. Minot
J. J. Boland	R. R. Stratton	E. L. Kickham	J. P. Monks
I. S. F. Dodd	MIDDLESEX NORTH	D. L. Lionberger	Donald Munro
C. F. Kernan	H. R. Coburn	D. S. Luce	R. N. Nye
BRISTOL NORTH	W. M. Collins	C. M. Lydon	F. R. Ober
W. H. Allen	D. J. Ellison	T. F. P. Lyons	J. P. O'Hare
J. H. Brewster	A. R. Gardner	Charles Malone	L. E. Parkins
R. M. Chambers	W. H. Sherman	F. P. McCarthy	L. E. Phaneuf
J. L. Murphy	M. A. Tighe	M. W. O'Connell	Helen S. Pittman
W. H. Swift	MIDDLESEX SOUTH	H. C. Petterson	W. H. Robey
BRISTOL SOUTH	C. F. Atwood	S. M. Saltz	G. C. Shattuck
G. W. Blood	E. W. Barron	D. D. Scannell	R. M. Smith
E. D. Gardner	W. B. Bartlett	J. W. Spellman	Augustus Thorndike, Jr.
H. E. Perry	S. M. Biddle	M. H. Spellman	E. F. Timmins
C. C. Tripp	G. F. H. Bowers	J. P. Treanor, Jr.	S. N. Vose
ESSEX NORTH	R. N. Brown	W. J. Walton	Shields Warren
E. S. Bagnall	R. W. Buck	N. A. Welch	Conrad Wesselhoeft
R. V. Baketel	E. J. Butler	NORFOLK SOUTH	C. F. Wilinsky
L. R. Chaput	B. F. Conley	C. S. Adams	WORCESTER
E. H. Ganley	C. H. Dalton	H. H. A. Blyth	J. C. Austin
H. R. Kurth	H. F. Day	R. L. Cook	Gordon Berry
P. J. Look	C. L. Derick	D. B. Reardon	W. P. Bowers
R. C. Norris	J. E. Dodd	H. A. Robinson	L. R. Bragg
G. L. Richardson	J. G. Downing	W. L. Sargent	P. H. Cook
A. F. Shea	C. W. Finnerty	PLYMOUTH	G. A. Dix
F. W. Snow	F. W. Gay	P. B. Kelly	E. B. Emerson
T. N. Stone	H. G. Giddings	P. H. Leavitt	J. M. Fallon
ESSEX SOUTH	H. W. Godfrey	G. A. Moore	E. L. Hunt
Bernard Appel	A. M. Jackson	D. W. Pope	E. R. Leib
C. P. Brown	E. E. Kattwinkel	W. H. Pulsifer	W. F. Lynch
C. L. Curtis	A. A. Levi	SUFFOLK	A. W. Marsh
S. E. Golden	F. P. Lowry	H. L. Albright	J. C. McCann
Loring Grimes	A. N. Makechnie	W. B. Breed	J. M. Melick
J. F. Jordan	R. A. McCarty	W. E. Browne	J. W. O'Connor
B. B. Mansfield	J. C. Merriam	C. S. Butler	R. S. Perkins
W. G. Phippen	Dudley Merrill	G. C. Caner	W. C. Seelye
E. D. Reynolds	C. E. Mongan	David Cheever	C. A. Sparrow
C. F. Twomey	J. P. Nelligan	M. H. Clifford	G. C. Tully
C. A. Worthen	Dwight O'Hara	Pasquale Costanza	R. J. Ward
FRANKLIN	L. S. Pilcher	R. L. DeNormandie	F. H. Washburn
F. J. Barnard	E. H. Robbins	Reginald Fitz	R. P. Watkins
A. H. Ellis	E. F. Ryan	Channing Frothingham	S. B. Woodward
W. J. Pelletier	J. W. Sever	M. N. Fulton	WORCESTER NORTH
H. G. Stetson	E. F. Sewall	A. A. Hornor	H. C. Arey
HAMPDEN	R. A. Taylor	H. A. Kelly	E. A. Adams
W. C. Barnes	H. W. Thayer	T. H. Lanman	C. B. Gay
W. A. R. Chapin	J. H. Townsend	R. I. Lee	J. C. Hales
E. C. Dubois	J. E. Vance		
P. E. Gear	Hovhannes Zovickian		
Frederic Hagler	NORFOLK		
G. D. Henderson	J. R. Barry		
E. A. Knowlton	Carl Bearse		
M. W. Pearson	M. I. Berman		
G. L. Schadt	H. M. Emmons		
MIDDLESEX EAST	J. E. Fish		
J. H. Blaisdell	David Glunts		
	B. T. Guild		
	D. L. Halbersleben		
	J. B. Hall		
	R. J. Heffernan		

## APPENDIX NO. 2

## REPORT OF THE EXECUTIVE COMMITTEE

The Executive Committee has had two meetings. The organization meeting, held on June 23, 1941, was presided over by the president of the Massachusetts Medical Society, Dr. Frank R. Ober. Dr. Edward P. Bagg, vice-president of the Massachusetts Medical Society, was elected vice-chairman of the committee. Dr. Michael A. Tighe served as secretary. Under the by-laws it was necessary that at the moment of organization, this committee should select by lot six men who would serve for three years, six who would serve for two years and six who would serve for one year. The selection so made is as follows:

## THREE YEARS

*Berkshire* John J Boland, Pittsfield  
*Franklin* Frederick J Barnard, Greenfield  
*Hampden* George L Steele, Springfield  
*Middlesex North* William M Collins, Lowell  
*Norfolk* Carl Bearse, Boston  
*Worcester North* John J Curley, Leominster

## TWO YEARS

*Barnstable* William D Kinney, Osterville  
*Bristol North* William H Allen, Mansfield  
*Bristol South* Edwin D Gardner, New Bedford  
*Essex North* Frank W Snow, Newburyport  
*Middlesex East* Kenneth L MacLachlan, Melrose  
*Plymouth* Pierce H Leavitt, Brockton

## ONE YEAR

*Essex South* Loring Grimes, Swampscott  
*Hampshire* Lucius B Pond, Easthampton  
*Middlesex South* Dwight O Hara, Waltham  
*Norfolk South* Daniel B Reardon, Quincy  
*Suffolk* Augustus Thorndike, Jr, Boston  
*Worcester* Ralph S Perkins, Worcester

It was voted by the Executive Committee to create the office of executive secretary. On nomination by the President, Mr Robert St B Boyd was elected to this office.

The second meeting of the Executive Committee was held on September 10, 1941. Out of that meeting have come certain recommendations which are herein presented to the Council of the Massachusetts Medical Society.

Hitherto the annual meeting of the Council has been held on the morning of the first day of the annual meeting. Occasionally the Council meeting has run well into the afternoon. This arrangement has deprived the members of the Council of the privilege of attending many of the scientific sessions of the annual meeting.

The Executive Committee, while taking notice of the self-sacrificing interest which the members of the Council bring to the purely business affairs of the Society, still recognizes the direction in which their chief interest lies. This committee, having in mind the importance of the annual meeting of the Council and believing that attendance at this meeting should penalize the members of the Council as little as possible, offers the following recommendations:

**Recommendation 1** The Executive Committee recommends that the Council of the Massachusetts Medical Society designate the first day of the annual meeting as the time of the annual meeting of the Society.

**Recommendation 2** The Executive Committee recommends that the Council of the Massachusetts Medical Society hold its annual meeting on the evening previous to the annual meeting of the Society.

The committee believes that adoption of these recommendations does not involve a breach of the bylaws. Under the bylaws, the Council has the right to name the time and place of the annual meeting of the Society. The only provision in the bylaws which has to do with the annual meeting of the Council is to the effect that this meeting shall be held on the day previous to the annual meeting of the Society.

It has come to the attention of the Executive Committee that serious thought is being given to the matter of the rehabilitation of those selectives who have been rejected because of remedial defects. The Executive Committee, through its secretary, has been approached in this

matter by Mr Curtis M Hilbard, director of the Committee on Health of the Massachusetts Committee on Public Safety. While this is not entirely a medical problem, it is to some extent. It would seem important that the Massachusetts Medical Society should participate, first, in the determination of the size of the problem and, secondly, in how best it can be solved.

**Recommendation 3** The Executive Committee recommends that the Council of the Massachusetts Medical Society authorize the appointment, by the President, of a committee of five, which committee shall be known as the Rehabilitation Committee.

There has been much discussion in the Executive Committee as to the number of years a foreign practitioner of medicine should be resident in Massachusetts before being permitted to take the examinations of the Massachusetts Board of Registration in Medicine. The Executive Committee is entirely familiar with the present regulation which requires that such practitioners shall be the possessors of first citizenship papers. While this committee knows that the Committee on State and National Legislation has already given thought to this matter, it nevertheless believes that this is a subject for further exploration.

**Recommendation 4** The Executive Committee recommends to the Council of the Massachusetts Medical Society that the Committee on State and National Legislation be instructed to study further the matter which has to do with the number of years a foreign practitioner of medicine should be resident in Massachusetts before being allowed to take the examinations of the Massachusetts Board of Registration in Medicine.

The Executive Committee has considered in detail and at great length a tentative set of bylaws under which it is proposed to set up a system of medical care costs insurance. These bylaws were presented to the Executive Committee by Dr James C McCann, chairman of the special committee of five. A copy of these bylaws accompanied the notice calling this meeting. They will later be presented to the Council through the report of the Committee on Public Relations. The Executive Committee commends these bylaws to a painstaking and earnest consideration.

It has also come to the attention of the Executive Committee that there is much confusion in the minds of many fellows of the Massachusetts Medical Society as to the proper interpretation of certain phraseology contained in Chapter V, Section 2, of the bylaws of the Massachusetts Medical Society.

The Executive Committee therefore submits the following resolution by means of which it seeks to have the Council interpret the language involved:

WHEREAS, The Massachusetts Medical Society is desirous that all skillful and ethical practitioners of medicine in Massachusetts shall be members of the Massachusetts Medical Society,

WHEREAS, Chapter V, Section 2, of the bylaws of the Massachusetts Medical Society provides the means by which practitioners in medicine in Massachusetts may become members of the Massachusetts Medical Society

WHEREAS, By the language involved in Chapter V, Section 2, of the bylaws of the Massachusetts Medical Society the Council of the Massachusetts Medical Society intends that it shall have accurate knowledge of the training, medical skill and ethical conduct of those

who seek admission to membership in the Massachusetts Medical Society;

WHEREAS, In the case of graduates of nonapproved schools, Chapter V, Section 2, of the by-laws of the Massachusetts Medical Society provides that the applicant for membership in the Massachusetts Medical Society shall have been in the practice of medicine for a minimum of five years;

WHEREAS, In establishing such a period of probation for graduates of nonapproved schools, the Council of the Massachusetts Medical Society intends that it shall have had opportunity to observe closely the medical skill and ethical conduct of such applicants; and

WHEREAS, In the case of most graduates of foreign medical schools who have been in the practice of medicine for five years in foreign countries, the Council of the Massachusetts Medical Society has no opportunity to know of the training or adequately observe the medical skill and ethical conduct of such medical practitioners; therefore, be it

RESOLVED, That the Council of the Massachusetts Medical Society interprets the phrase "who has practiced for a minimum of five years," as appearing in the by-laws of the Massachusetts Medical Society, Chapter V, Section 2 (b), to mean what is meant by the phrase, who has lawfully practiced for a minimum of five years in the United States; and be it further

RESOLVED, That the Council of the Massachusetts Medical Society shall be considered to have accurate knowledge of the medical training and medical skill of such graduates of foreign medical schools who have practiced medicine in foreign countries for five years and who are eminent in the profession of medicine and well known to the Council of the Massachusetts Medical Society for their scientific attainments, provided such practitioners shall have satisfied the Council of the Massachusetts Medical Society that their medical practice has been ethical according to the standards as set down in the *Code of Ethics* of the American Medical Association.

MICHAEL A. TIGHE, *Secretary*

#### APPENDIX NO. 3

##### REPORT OF THE COMMITTEE ON MEMBERSHIP

The committee recommends:

1. That the following named three fellows be allowed to retire under the provisions of Chapter I, Section 5, of the by-laws:

Collins, William J., Northampton  
Eldridge, David G., Milton  
Mason, Nathaniel R., Marblehead

2. That the following named three fellows be allowed to resign under the provisions of Chapter I, Section 7, of the by-laws:

Catinella, Paul J., Rochester, Minnesota  
Macomber, Donald, Boston  
Strong, Archibald M., New York City

3. That the dues of the following named two fellows be remitted under the provisions of Chapter I, Section 6, of the by-laws:

Ford, John F., Roslindale, 1941  
Shukle, R. M., Boston, 1938 and 1939

4. That the following named five fellows be allowed to change their membership from one district society to another without change of legal residence, under the provisions of Chapter III, Section 3, of the by-laws:

FROM ESSEX SOUTH TO MIDDLESEX EAST  
Ward, Joseph O., Saugus

FROM MIDDLESEX SOUTH TO SUFFOLK  
Brailey, Allen G., Newton Highlands

FROM NORFOLK TO SUFFOLK  
Auglem, Thomas J., Milton

FROM NORFOLK SOUTH TO SUFFOLK  
Williams, Robert H., Squantum

FROM SUFFOLK TO MIDDLESEX EAST  
Chisholm, Julian F., Jr., Boston

5. That the following named six fellows be recommended for readmission under the provisions of Chapter I, Section 10, of the by-laws:

Chayet, Jacob, Brookline  
Dushan, Sidney S., Mattapan  
Messer, Edward C., Dorchester  
Peterson, Reuben, Duxbury  
Pulsifer, Nathan, Lowell  
Sannella, Theodore, Boston

G. COLKET CANER, *Chairman*

#### APPENDIX NO. 4

##### REPORT OF THE COMMITTEE OF ARRANGEMENTS

At a meeting, as required by Chapter VII of the by-laws of the Society, the Committee of Arrangements, in co-operation with Dr. Ober, voted, after due deliberation, to hold the next annual meeting of the Society in Boston at the Hotel Statler on May 26 and 27, 1942. If this convention according to custom were to be held on the second Wednesday of June (June 10), there would be a conflict with the annual meeting of the American Medical Association in Atlantic City; this did occur in 1931. Pending your authorization, therefore, it was decided that there should be no such conflict.

The Committee of Arrangements endorses firmly the proposal of the Executive Committee, which you have approved this morning, that the next annual meeting of the Council be held in the evening preceding the first day of the annual meeting of the Society, according to present plans on the evening of May 25, 1942. Such a change would not only permit councilors' attendance at program functions which they cannot enjoy as it is, but also it would allow them to advance likewise the date of the annual business meeting of the Society by one day to the first day of the convention. Then the program of the second day could proceed without interruption.

Reservations have been made tentatively at the Hotel Statler, whose greater accommodations are sufficient for all our usual or anticipated demands and where a better attendance is more likely. Concerning other important details, like progress with the composition of the speakers' program, no satisfactory report can be presented at this time since such arrangements are so contingent on your decisions of today.

For future meetings it might be a time-saving measure for the Council to declare that it expects no conflict in

the dates of the two conventions and that any invitations from district societies to hold the annual convention outside Boston must be received by the Committee of Arrangements well before the annual meeting of the Council. Please consider these suggestions as a part of this report of the Committee of Arrangements but not as motions for action.

This report ends with the resolution

That the next annual meeting of the Massachusetts Medical Society be held at the Hotel Statler in Boston on May 26 and 27, 1942

WILLIAM T O'HARRIS *Chairman*

## APPENDIX NO 5

### REPORT OF THE COMMITTEE ON STATE AND NATIONAL LEGISLATION

**Organization** This committee was appointed at the annual meeting in 1940. There was a central organization of the following members: Henry C Marble, David L Lionberger, Brunard F Conley, Charles A Robinson and Earle M Chapman.

In each of the several districts a similar committee was appointed at their annual meetings, and during the past year of service, the following physicians have acted as chairmen of these committees: Dr D E Higgins, Dr P J Sullivan, Dr W M Stobbs, Dr E F Cody, Dr Edward Ganley, Dr C A Worthen, Dr H G Stetson, Dr W A R Chapin, Dr E E Thomas, Dr K L MacLachlan, Dr Michael A Tighe, Dr B F Conley, Dr E L Kickham, Dr J E Knowlton, Dr George A Moore, Dr E M Chapman, Dr L M Felton, Dr J V Gallagher, and Dr R F Bachmann.

Because of the geographical position of the central committee, it fell on this committee to attend most of the hearings at the State House, but at various times it was necessary to call in members of the other committees for assistance, and they all worked well in conjunction with us in carrying the legislative work of the Society into every corner of the State. It was because of this far flung organization and effective work that we were able to accomplish what we did.

The Society engages the services of a legislative reporting bureau which reports to us all bills that have been entered and, in many cases, furnishes us with type written copies of the bills even before they are printed. It so happened during the early part of 1941 that on certain occasions a bill went to hearing before a legislative committee even before that bill had been officially printed. From this it must be clear that it was difficult to keep up with the flow of hearings. As each bill was entered, it was assigned to one of the members of the central committee for study. He read it, and thereafter reported with his recommendations at a meeting of the central committee, at that time the policy that should be followed was worked out. Immediately after this was done the first legislative bulletin was published, which was sent to all the district legislative committees. Thereafter it was found that many bills had been entered that did not appear to be of interest to the Society because of the obscure title, and on several occasions it was not until a day or two before the bill was heard that we had knowledge of its existence, or were aware of the fact that it had medical implications. All this required hasty preparation and many telephone calls and hurried conferences.

After filing, each bill is assigned to a committee by the speaker of the House. The committee puts a date for

the hearing. There may be many other hearings on the same date before the same committee. It is the duty of the committee and the legislative counsel of the committee to be present at all these hearings and to furnish proper evidence in the form of speakers to present the case of the Society.

After the hearing, the petition is written into the form of a bill and is presented to either the House of Representatives or the Senate. If, however, the bill calls for the expenditure of public funds, it must further be heard before the Committee on Ways and Means before going to the floor of the House or Senate. Any of these committees may amend, alter, change or entirely rewrite the bill. After the bill has been acted on in one branch, it is then referred to the other, where substantially this same program is repeated, and even in the case of a relatively unimportant petition, it must be carefully and diligently followed from beginning to end. To accomplish all this is a full time job for at least one man, and a large part time job for a legislative counsel.

If you will refer to the legislative bulletin, you will note that the various bills fall into several classes:

**Medical education** This includes medical schools, medical training, requirements for practice, and control of matters of medical education. Into this class fall S 485, S 560, H 114, H 272, H 611, and H 1722. We might say that it has been the policy of the committee to do everything in our power to improve and to safeguard the laws governing the practice of medicine. The bill establishing the Approving Authority to regulate medical schools has been in force since January, 1941. Up to this date, we have been unable to obtain a report.

**Nurses and nursing education** The history of the effort by the Nurses Association to have a separate Board of Registration is long. However, the nurses' registration bill has been entirely rewritten from the form in which it was presented at first and has been passed through the Legislature and is now in force. In brief, there is a separate board of registration for nurses. There is, in addition, an advisory council with power to control matters of nurses' education and to approve hospitals having training schools. This further is expanded to include attendants. It is our feeling that this will be a satisfactory and useful bill.

**Hospitals** A bill was presented by the Massachusetts Hospital Association, which bill we were glad to approve, it gave the Department of Public Health authority to license general hospitals. This bill started as H 1232 and was rewritten as H 2528. In the closing days of the legislative session this bill was passed and signed by the Governor.

**Public health** The major item was the enactment of the Massachusetts Medical Society bill for the prepayment of medical care. This bill passed the Legislature, as nearly as I can determine, without a dissenting vote and is now a law.

Other bills were presented relative to premarital medical advice. H 460, providing for premarital examination by a qualified physician was passed and signed by the Governor on August 2. The annual anti-vaccination bill was presented and again given leave to withdraw. In general the committee sought to co-operate with the Department of Public Health in all constructive measures.

**Drugs and poisons** Several bills were presented by the Department of Public Health relative to food and drugs. In all of these we supported the department

An effort was made to restrict the sale of barbituric acid and its derivatives; this was not passed. A bill to limit the sale of pure ethyl alcohol was presented, but was defeated.

It is my considered opinion that the work of this committee in the future can be much simplified if many of these matters which we now have before us are considered and made part of a long-term policy of the Society. We should proceed to lay out a program of progressive public-health legislation that will embody most of the matters that have been here covered. It is further my opinion that this should be given to the Society long enough ahead so that it may have an opportunity to give the program careful study. I am entirely confident that any such long-range program would be welcomed by the Legislature. If the Medical Society offers such a progressive program, I am sure that it will forestall the filing of many time-consuming petitions.

HENRY C. MARBLE, *Chairman*

## APPENDIX NO. 6

### REPORT OF THE COMMITTEE ON PUBLIC RELATIONS

The Committee on Tax-Supported Medical Care, reporting through the Committee on Public Relations, is stimulating progress toward the setting up of district committees for improvement in the distribution of medical care in this field. The secretary of each district society and the delegates to the Committee on Public Relations are endeavoring to have the district committee authorized by the first meeting of the district society, thus carrying out the vote of the last Council meeting. Several local plans have been started on the initiative of organized medicine, and information regarding these is being distributed as fast as it becomes available.

The McCann Committee presents through the Committee on Public Relations the by-laws for a corporation to be known as the "Massachusetts Medical Service Corporation." These have been considered by the Committee on Public Relations, and it recommends their adoption as a basis for discussion, with the understanding that after constructive criticisms here and from other sources, they will be again presented to you for final approval before adoption. Rules, regulations and contracts with physicians and subscribers have not yet been prepared.

E. S. BAGNALL, *Secretary*

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### REPORT OF THE COMMITTEE ON PREPAID MEDICAL-COSTS INSURANCE

For your consideration, the committee is presenting by-laws, which represent the most vital step in establishing a corporation for prepaid medical service. Within a set of by-laws are established the essential characteristics of a corporation; furthermore, by-laws can guarantee or forfeit very valuable rights and powers with reference to the practice of medicine.

With our presentation today there has been distributed a printed form of the by-laws. Although it does not constitute a printed final, an unalterable form for you to act on, these by-laws indicate in principle the type of corporation that your committee believes conforms with the intent of the majority of the Council and the Massachusetts Medical Society.

As you know, several years ago the Council decided by a majority vote to embark on a program of prepaid

medical insurance. Under the able chairmanship of Dr. Thomas H. Lanman, this purpose was forwarded when an enabling act was signed by the Governor on May 22, 1941. The purposes behind your decision should necessarily be considered in a discussion of the character of any program on which we embark. Before going over the details of the by-laws, I wish, therefore, to give you the basic thoughts and the philosophy in the mind of your committee when it drew up the by-laws.

The purpose in establishing such a corporation is twofold. The first has reference to the public at large, particularly the low-income segment of the middle-class group. Owing to insecurity of work and the lack of fixity of income in our present industrial age, the members of the low-income group claim that medical costs often attain proportions that are difficult to meet. In attempting to meet this demand for relief, we think that there are two objectives to guide us. First, if we seek to help them ameliorate the cost of medical care it can be done on the widely established principle of insurance, which dilutes cost on the basis of distribution of risk over a large group; secondly, by budgeting and prepayment, we can make it possible to take care of unforeseen medical costs ahead of time. It is the opinion of your committee that you have not committed us to seek other ends, which would only act to complicate the program and jeopardize any chance for success. The second purpose is personal, but may be expressed in terms of enlightened self-interest: we openly seek to diminish the hazard of compulsory health insurance. The chances are that, if our program succeeds and is widely accepted by subscribers, we can ward off this threat. However, there are two important considerations. First, the proponents of compulsory insurance may urge that we have not and cannot enroll sufficient subscribers except by appeal to the principle of compulsion—they even threaten to apply this philosophy in the form of compulsory savings. The second point which may be a factor in failing to ward off compulsory insurance is the result of a demand for contributions from the employer and from the State in payment of the premiums. On this basis there may be a demand for participation by the State in the activities of the corporation. However, if we can enlarge adequately the subscription lists and the funds coming from subscribers, I think we shall find little difficulty in warding off compulsory insurance.

There is also another very important principle to keep in mind with reference to compulsory insurance, namely, that any legislative program which is to be established is usually based to a large extent on pre-existing conditions. Hence, if a compulsory-insurance program were worked out in the Legislature it would in all probability be based on our existing prepaid insurance corporation. In England, for example, the system is handled by the insurance carriers that were already underwriting the voluntary schemes. If by your initiative we establish a satisfactory program, or a relatively satisfactory one, we can assure to ourselves control over the purely medical aspects of the program. We shall have conserved to the physicians of the State certain rights and privileges inherent in medical practice, which we maintain belong to us. If a program of compulsion is unhappily imposed on us later, on the basis of established corporate practice, we can still probably save to ourselves these rights and privileges, and a satisfactory basis for practice.

Having reviewed this background, I now suggest that there are definite steps to be taken in succession to establish such a corporation on a sound basis. The first step, of course, is to procure an enabling act, which we



already have done. The second is the adoption of by laws that will establish the character of the corporation, and thus we now seek, the third is the preparation of rules and regulations, which must be based on established by laws. The fourth is a study of the actuarial background in Massachusetts, in which task we shall profit greatly by the experience of other states which have already embarked on similar programs, and the last step is the preparation and offering of specific contracts.

To proceed with the writing of rules and regulations, your committee must know the type of corporation that physicians will accept, so that subsequent steps may be referred to a basic pattern. That is why it is urgent for us to arrive at a decision on this matter of the bylaws, which will create the pattern. There are three fundamental concepts that must always be kept in mind when writing the bylaws of such a potentially powerful corporation, so that we may not do damage to our own legitimate self-interest. These concepts are as follows: first, we are embarking very definitely on a business venture of great magnitude; secondly, we do so on the basis of establishing a corporate structure; and thirdly, so far as medical practice is concerned, it is to be done on a contract basis. So we are embarking on extremely troublesome waters, which involve us widely in the corporate and contract practice of medicine.

With reference to the business aspect of this program we should look at it from the vantage point of its parallel to the business structures that surround us. Thus we may clearly visualize our rights as well as our obligations, and guard against missteps which would lose us certain privileges and rights that are identified with the practice of medicine.

Any business structure is looked at from the viewpoints, first, of promotion; secondly, of organization and management; and, thirdly, of finance. Certainly this program is one that is sponsored and promoted by the physicians. With reference to its organization and management, there is one basic principle that we must always keep in mind lest we be misled: namely, that the professional aspect of such a corporation transcends its administrative and monetary aspects. When an ordinary business corporation is established, the basic problems are administrative. In seeking the basic problems in our corporation, let us draw a parallel with workmen's compensation insurance in which the professional or medical aspects require 85 per cent of the time to run the program. If we compare a medical service organization, which is devoid of all the legal matters pertaining to liability, the value of services, cash benefits and so forth, with compensation insurance, which has all these features, certainly the medical or professional aspects of the former will loom even larger than those of the latter.

Then, too, I think we must insist that the contribution of the physician transcends the contribution represented by the premiums of the subscribers, which are only a benefit or claim for completion of the contract. The subscriber contribution is not so-called risk capital, any more than your premiums to a stock life insurance company represent risk capital or an ownership claim. We are contributing the body of knowledge possessed by the whole medical profession, and the acquisition and use of that knowledge and skill by the individual physician. This knowledge, skill and practice represent, we should insist, capital knowledge that is of major importance in the operation of any medical service corporation. Certainly our knowledge is patentable—consider insulin and viosterol, however, our ideals do not permit universal patenting, and our progress is a universal gift to mankind. If the patents

of a business corporation represent some of its most valued assets, certainly the knowledge and technical skill of the physician should represent a major capital interest in this corporation. So that as your committee tried to preform the character of this corporation, it seemed equitable to us that on the basis of business practices, the right of physicians to control judiciously this corporation should not be questioned.

With reference to the establishment of a corporate structure, we must give serious attention to the constitution of corporate structures and to the medicoeconomic significance of practicing medicine under a contract with a legal entity known as a corporation.

The corporation that we envision may be potentially a most powerful organization. If it should bring in a large proportion of the seven thousand resident physicians of Massachusetts if it should bring in somewhere around 50 per cent of the 4,000,000 of the residents of the State, and if it should bring in all the funds that are turned over at present in the distribution of medical services between these groups, it could be one of the most powerful corporate structures in Massachusetts.

The one most important thing to keep in mind is the question wherein will control of the corporation reside? By what means will the physicians maintain their proper control of this corporate structure? Let us turn to the common business corporation to sense just what we are doing, keeping ever before us the truism of corporate practice, namely, that wherein resides control of the board of directors, there resides control of the corporation.

Corporations are of two basic types, the profit corporation and the nonprofit corporation. Under the profit corporation there are three types so far as control of the board of directors is concerned. There is control by majority stock ownership, in which a sufficiently large block of stock is in the hands of one man or of a small limited group of men, so that he or they can dominate the board and the practices of the corporation. This power is achieved through the right to nominate and elect and to remove the board of directors. The directors are representatives of the stockholders who determine the practices of the corporation for the benefit of the stockholders. They are completely amenable to control by the owners or the majority stockholders.

Coming from a corporation in which there is this minority stock interest we come to a corporation in which there has been such dilution of stock ownership by wide sale that there are no blocks of shares sufficiently large to create a majority stock ownership. This results in minority stock control. Immediately one begins to see how dangerous such a development in corporate structure may be for the owners of the corporation. A minority block may be insufficient in size to control the conduct of the business by controlling the acts of the board of directors. Such a board may work its will as it pleases, even defying the demands of the owners. The classic example of such defiance is the Standard Oil Company of Indiana. Here the chairman of the board of directors, Colonel Stewart, defied John D. Rockefeller, Jr., representing the chief minority stock interest, in the conduct of the corporation, so that Mr. Rockefeller had to spend millions to procure proxies sufficient to enforce the will of the owners on the management. Herein we see the danger that comes when the affairs of the corporation are placed in the hands of a board of directors not completely subject to the will of the owners, or to the will of those who have rightful claims to priority in the corporation.

Next we come to what is called management control of a corporation, which is best exemplified by the American

can Telephone and Telegraph Company. I have a younger brother who is a general manager and vice-president of one of the subsidiaries of this corporation, and I know just how much attention would be paid to any representation to him or his associates by a stockholder in the matter of administering the corporation. The stockholder would be received with the greatest courtesy, but when he left the office the matter would be pigeonholed. The chief characteristic of this form of corporate structure is that absolute control is exercised by a board of directors; the stockholders are completely impotent because of dilution of their powers by the excessive distribution of stock. Thus the owners of a corporation can lose control of the corporate structure that they own and have created. This situation parallels our own, in the absence of a stock issuance by our corporation. We now see why we must procure control.

Moving to the nonprofit corporation, we enter the field in which our medical-service corporation will be chartered. In the usual philanthropic, nonprofit institution, there is no great concern over where control of the corporation resides, or what extent of control the owners of the corporation have over the board of directors. For instance, the Home for the Blind in Worcester has been endowed with funds and established, and there is little more to be done other than to conserve the funds and to carry out the corporate purpose of maintaining a home for the blind.

Next in the line of nonprofit corporations from which we can draw instruction is the Blue Cross. There are vital differences between the Blue Cross and what will be our corporation for medical service. The Blue Cross has been established as a sort of insurance go-between for the patient and the hospital corporation. The Blue Cross has no power over the individual corporate structure of hospitals; the individual hospital corporation is still in full control of its own destiny. The hospital directors are in no way controlled by the Blue Cross.

But when we move on to the formation of a medical-service corporation, a nonprofit corporation, we cannot afford to take the viewpoint that its setup is as innocuous as that of the Blue Cross. The physicians of the State, who are in complete control of the profession of medicine, are planning to place a large part of their practice under the control of a corporation by the medium of a contract. There is no stock ownership so that we cannot control this corporation through the medium of stock ownership. We have to adopt other measures of control if we are to protect our inalienable interests.

Those of us who have been interested in the philosophy of corporate structure in America know that in recent years two hundred corporations have achieved control of 50 per cent of the entire corporate wealth of the United States and control some 15 per cent of the employed workmen of America. I shall cite one authority on the growing separation of ownership in a corporation from control, so as to impress you with the importance of control—the statement of Justice Brandeis in the case of *Liggett versus Lee* (288, U. S. 517 [1933], p. 548):

Ownership has been separated from control; and this separation has removed many of the checks which formerly operated to curb the misuse of wealth and power. And as ownership of shares is continually becoming more dispersed, the power which formerly accompanied ownership is becoming increasingly concentrated within the hands of a few. The changes thereby wrought in the lives of the workers, of the owners, and of the general public are so fundamental and far-reaching as to lead these scholars to compare the evolving "corporate system" with the feudal system;

and to lead other men of insight and experience to assent that this "master institution of civilized life" is committing it to the rule of plutocracy.

The control that we should establish over the corporation ought to be based, first, on this background of principles and facts that we have just discussed; secondly, it should be governed by the principle that all distinctly professional matters should be kept in the hands of the physicians; thirdly, the organization should be so arranged that in the future such power over professional matters should not be allowed to get out of the hands of physicians; and fourthly, we should keep in mind the necessity of procuring an intelligent representation of the public in this program.

Turning now to the diagram or pattern of our corporation, there are three major subdivisions of the corporation: that division wherein we establish a voting membership; that wherein we establish a managing body or board of directors; and that wherein we create for the district societies the very highest degree of home rule by establishing units, which will carry out locally the purposes of the corporation.

In brief outline, we have established the Executive Committee of the Massachusetts Medical Society, composed of twenty-three members, as the voting members. This is the only point at which physicians, who are entitled to controlling powers, can enter this corporation, other than by comprising a majority of the directors. The latter has many undesirable aspects, which I shall discuss later. We first had all the members of the Council as voting members, but as we discussed the problem we thought that for the sake of functioning satisfactorily, it would be better to have a small group of physicians as voting members, who would be definite representatives of the Society as a whole, because we must visualize that once this corporation is established it will practically run itself. The Executive Committee will be more or less what you might call the watch-dog of the system, seeing that nothing which jeopardizes the rightful and proper interests of physicians takes place. This is the group in the corporation which has control of the corporation by virtue of the powers granted them in the by-laws: power to appoint directors; power to remove directors; sole power to change the by-laws, which perpetuate their powers; and power to review vital actions that will arise.

The number of the Board of Directors, the second group on the diagram, has been set at fifteen. One third shall be physicians; one third, as required by the enabling act, shall be subscribers; and the other third may be made up of prominent laymen. If this corporation assumes the proportions that we believe it well may, there are certainly going to be distinct problems of administration and of finance with which the directors must concern themselves expressly. Hence, we must have a setup that will allow us to call on suitable persons in the community to assist in carrying out these parts of the corporate responsibility. To return to the alternative proposition, if we were to seek to control the corporation by putting in a majority of physicians as directors, we should create a situation wherein we could not call on that powerful, intelligent body of citizens whom we need to assist us. Let us assume there is a board of fifteen directors. If a third, or five, are subscribers, and a majority, or eight, are physicians, one would not secure, we believe, in the two remaining appointments sufficient representation of those lay people from whom we need so much help. So in rejecting, as impracticable, control by a majority of physicians as directors, we have substituted what seemed to us to be a fair and effective setup, in which the physicians will have

unquestioned control of their own professional concerns. This is achieved by allocation of control over such questions to the Central Professional Service Committee, which is composed, with one exception, of physicians. We have delegated to them sole power to initiate action on vital medical matters. With reference to such matters, only these physician directors can initiate alteration of the rules and regulations, which will emanate from this body, the Council of the Massachusetts Medical Society. As the doctors are the producers and distributors of medical care, a board of directors should properly be our representatives. Since we are creating a board of directors with lay and subscriber members, we are justified in protecting our quasi-ownership rights by this indirect method, thus keep

Massachusetts Medical Society. That does not commit us one way or the other on the election of the directors, so we choose to elect all of them. If the subscribers find some way of nominating their representatives, certainly in view of our power to elect, this is acceptable. When I say our power I mean the Executive Committee's power to elect the directors, a majority of whom are acceptable to them. They have power to terminate directorship. This is nothing unusual in corporate practice, indeed, in all business corporations it is stated that the members may, with or without cause, terminate the tenure of office of any member of the board of directors.

This draft states definitely that amendments to the bylaws are in the hands of the members of the corpora

## MASSACHUSETTS MEDICAL SERVICE CORPORATION

### MASSACHUSETTS MEDICAL SOCIETY

- 1 Creates corporation
- 2 Controls it by direct elections through the voting members

### VOTING MEMBERS OF CORPORATION

(THE 23 MEMBERS OF THE EXECUTIVE COMMITTEE OF THE COUNCIL OF THE MASSACHUSETTS MEDICAL SOCIETY)

- 1 Elect Board of Directors
- 2 Terminate directorship
- 3 Change by laws
- 4 Receive notice of changes by the Central Professional Service Committee

### BOARD OF DIRECTORS

(5 PHYSICIANS 5 SUBSCRIBERS 5 UNSPECIFIED)

- 1 Supervises and controls administrative matters with
  - a Medical director and assistants
  - b Administrative Committee(?)
- 2 Supervises and controls financial matters with
  - a Administrative group
  - b Finance Committee(?)
- 3 Appoints Actuarial Research Committee (at least 3 members)
- 4 Appoints Central Professional Service Committee (5 members of whom chairman and 3 others must be physicians) this committee has sole power to initiate changes reporting them to the voting members on the following:
  - a Extent of medical benefits
  - b Basis of compensation
  - c Standards of medical care
  - d Discipline of physicians
  - e Qualifications of specialists
  - f Extension of income groups

### DISTRICT ADMINISTRATIVE UNITS

(MAJORITY PHYSICIANS CHAIRMAN PHYSICIANS ELECTED BY DISTRICT SOCIETIES)

- 1 District administrative committees
- 2 District professional service committees (all physicians)
  - a Have sole power of concurrent action with the Central Professional Service Committee
  - b Supervise locally the quality of medical care
  - c Discipline local physicians
  - d Determine qualifications and furnish lists of local specialists for the benefit of subscribers (optional)

ing vital medical matters in the hands of bona fide representatives of the medical profession.

In the local communities we have established district administrative units, the third section of the diagram. Each is composed of not more than nine individuals, of whom a majority must be physicians engaged in active practice. We have arranged for the chairman to be a physician, since any committee is apt to be strongly influenced by the chairman. Certainly we must guard this opportunity of protecting the medical aspect of local problems. Under the setup, there is a district administrative committee endowed with administrative powers only, and a professional service committee composed of physicians, which has complete control of all medical matters.

To go into more detail concerning the powers of these three segments of the corporation, the members of the Executive Committee of the Society (young members) are destined to control it. They have given to them the power to elect the board of directors. The enabling act states that a majority of directors shall be approved by the

union. That provision is based on accepted legal practice. We are doing some things a little differently from the usual practice, but certainly we are doing something different when we place the practice of medicine in the control of a corporation. This grants to us control of the elemental provision that any change in these vital matters shall be initiated by the physicians. It also preserves to the Massachusetts Medical Society control through its young membership, which has been vested in the Executive Committee of the Society.

The fourth provision is that the young members shall receive notice of changes contemplated by the Central Professional Service Committee. It is stated in the bylaws that the president of the Massachusetts Medical Society be notified, but I think it might be well to change the designation to the young members, who include the president of the Society, thus all the members would receive notice of any pending change. This whole group shall receive a thirty-days' notice of any change in the essential medical matters, passed on by the Central Professional

Service Committee. It is provided in the by-laws that any three members of the Executive Committee may call a meeting of the members so that if by mischance any questionable act has occurred or is contemplated by any group in power, a meeting of the members may be called to discuss that change. I think we have preserved to the physicians an adequate measure of control of the corporation, since the members have power to withdraw written approval of the majority of the directors, or even to terminate their tenure of office, at any time.

Coming now in detail to the Board of Directors, with reference to the provision for one-third subscribers, there is one fact which interested the group when we were discussing this set of by-laws—which, by the way, has been approved in principle by the Commissioner of Insurance. The counsel for the Commissioner pointed out to us that at one point in its existence the financial sheet of the Blue Cross was in such shape that, but for the wide subscribers' interest in the corporation, its activity might have been discontinued. So that in the early period of its life, our corporation should have a protective subscriber interest, which will help to tide us over the period when the financial status of the corporation will be subject to quite careful scrutiny by the Commissioner of Insurance.

With reference to the other third of the directors, as I have said, if this program develops successfully we shall need capable public-minded citizens in this corporation. The by-laws are drawn in quite general terms not committing the corporation to questions of what committees shall be formed. We believe we should permit the directors to meet and to organize themselves as they find the requirements of the situation demand. We should not tie them down. In the by-laws we have, in general terms, made it possible for them to establish such committees as they find necessary to run the corporation. We have not concerned ourselves in the by-laws with the problems of the medical director, because we cannot now discern the respective duties of the medical director and the Board of Directors. Their functions should not be strictly limited in the by-laws, and must, of course, be worked out with experience.

In the by-laws, however, we do commit the Board of Directors to establish two committees: the Actuarial Research Committee and the Central Professional Service Committee. We think that the Actuarial Research Committee should be established for very definite reasons. There is no sound actuarial basis for setting up such a program as this: it is purely experimental. In this connection, I quote from an address by Mr. W. A. Milliman, assistant actuary of the Equitable Society, speaking in New York City before the Actuary Society of America. He said, "Despite the enormous amount of effort that has gone into studies of the cost of insuring medical care, there is very little data on which an actuary could rely in calculating the costs of these benefits." I also have a report of the Committee on Economics of the Canadian Medical Association, which was made as far back as 1934; on the subject of actuarial experience, it states, "Sickness risks do not lend themselves to actuarial calculations."

Even though a capable board of directors might plan to appoint such a committee, we thought it best to require the appointment of such a committee immediately, since our whole welfare is at stake in this project. That would assure us a sound study of actuarial bases in so far as they can be made from the very beginning of the corporation's life.

The other provision of the by-laws binds the directors to establish the Central Professional Service Committee. There is also provision in the by-laws for delegating to this committee sole power to initiate all changes in the

rules and regulations concerning vital professional matters. This retains in the hands of the profession control of those matters that the English physicians at first lost under compulsory insurance, and then recovered only after years of bitter struggle.

While we studied the probable functioning of a medical-service corporation, we selected six functions (designated "a" to "f") of the Central Professional Service Committee as matters of vital medical importance over which physicians should be entitled to control as the quasi-owners of medical practice. So far as it is possible to designate "property rights" in a professional service, these functions seem to cover our property rights. Such rights have been defined as "control of access to the instruments of production." These functions infringe on the right of the individual physician to practice his profession; and they relate to changes of policy by the corporation which might jeopardize his security in such practice.

Let us consider the subheadings in detail. (a) *Extent of medical benefits.* From the experience of the Blue Cross we know that problems relating to how much x-ray examination, how much anesthesia and how much of any other special service shall be included in a sanely rounded program must arise. Only physicians are equipped to solve such problems. (b) *Basis of compensation.* This does not relate to how much shall be paid specifically for a certain service. It has reference to the fact that only physicians are qualified to determine what the proportionate return for an appendectomy as compared with a resection of the colon or the home treatment of pneumonia shall be. (c) *Standards of medical care.* This has always been the special province of the medical profession, and our corporation will be based on our ideal of ever-improving standards of medical care. (d) *Discipline of physicians.* This relates only to handling the small 2 or 5 per cent of the profession who welfare experience has revealed will intentionally abuse the corporation by overtreating, over-visiting and so forth. We simply believe that such discipline should never be the province of laymen, as it is in some foreign compulsory insurance schemes, but that physicians only should be allowed to judge practitioners of medicine in these matters. (e) *Qualification of specialists.* This concerns only allocation of authority. It assures us that if, as and when the Massachusetts Medical Society acts on this matter, then under our corporation the matter will be handled by properly accredited physicians and not by laymen. No action on this matter is entailed by acceptance of these by-laws. (f) *Extension of income groups.* The Council has already voted that any determination or extension of income groups privileged to receive benefits from the corporation shall be voted on by the Council. This action is safeguarded by this provision and other provisions in the by-laws.

In the local professional-service committees, the right to act with the Central Professional Service Committee on such of these headings as have important local significance has been established. These include the supervision of the local quality of medical care, the local discipline of offending physicians, and the local handling of the specialist problem, when the society shall have decided on a course of action.

I am briefly going through the by-laws to point out the sections that carry out the purposes we have in mind. Of the 350 lines in these by-laws, roughly 200 lines are concerned with purely legal matters, whereas only 150 lines are pertinent to vital medical aspects. I shall indicate these pertinent lines.

Article II, Section 1, establishes the members of the Executive Committee of the Massachusetts Medical Society

as the young members of the corporation. Section 4 gives power to three of the committee to call meetings whenever they believe that action should be taken.

Article III, Section 1, gives to the Board of Directors the necessary powers to manage the corporation, and it states the composition of the Board of Directors. Section 3 gives the members the voting control for the removal of directors if it is deemed necessary. That is one point where the Commissioner of Insurance has reserved a question. He has not yet committed himself, but he has reserved the right to question whether the phrase with cause should or should not be inserted, nothing more vital than that. As I have already said, most business corporations can remove directors with or without cause. Section 7 allows the Board of Directors to adopt rules and regulations subject to the conditions of Article IV. That simply means that any rules and regulations that are primarily established will not be modified if they relate to the vital medical matters unless initiated by the Central Professional Committee and reported by it to the Executive Committee of the Society (voting members). Section 9 establishes the general power of the directors to delegate power so far as they see fit to committees and officers, but subject to such regulations as may be adopted by the board and restricted by the provisions of the by laws.

Article IV, Section 1, is to be changed as follows: "There may be appointed such committees as the directors deem necessary, and there shall be appointed an actuarial research committee and a central professional service committee. This simplifies the problem of appointive power. Section 2 gives, so far as we could assure it, complete control in vital medical matters to the Central Professional Service Committee, and thus indirectly to the Massachusetts Medical Society through its chosen representatives. Section 3 specifies the fact that only in this committee shall action on these vital medical matters be initiated. Section 4 simply provides a means for setting up as far as a basis as could be established for handling disputes or, rather, abuses by physicians. It does not carry through the final action, which is determined by the enabling act, which requires that action shall go to a special committee consisting of the Commissioner of Insurance, the Commissioner of Public Health and the Attorney General. But by the provision of the by laws, many minor disputes may be quickly disposed of without loading busy public officials with the innumerable little problems that must necessarily arise. Sections 6 and 7 relate to the establishment of the Actuarial Research Committee, to which shall be submitted all questions relating to actuarial studies. Article V relates to purely legal matters, and any question there should be referred to a lawyer, nothing vitally affects the pattern of our corporation.

Article VI, Section 1, relates to the action of each district society, to which, if this program is going to succeed, such matters should eventually be referred. Section 4 designates a subordinate local professional service committee to act in an advisory manner in conjunction with the Central Professional Service Committee.

Article VIII makes it possible for us if we wish, and as the other states have found it advisable to do, to offer limited policies in addition to complete medical service policies. When the income level is established by the Council, people below that level can get complete medical service contracts, above that level people may buy a policy for which they will receive compensation from the corporation. But the limited contract in no way binds the physician in his charge to the patient, so that the present relation which exists between the physician and the patient continues to hold. By this means we make an effort

to reach the higher income group, taking care however, to impose certain restrictions, which do not obtain in the lower income group. As our approach to the lower income group depends on the good will of the upper income group, we win their support by a limited subscribers' contract. Section 5 is a general provision included so that, if at any time it is the will of the Council to permit certain charitable organizations, welfare boards or other groups to participate in the payment of premiums, this may be done without discussion or change in the by laws.

Under Article VII, Section 3 there is a phrase at the end that may be difficult to understand. I refer to, "He shall not have the right to refuse to accept a subscriber as a patient or to continue treatment of a subscriber for the sole reason that he is a subscriber." The only reason for the statement is that if we are going before the public with an appeal for subscriptions, they will insist that the subscriber have this protection. As our lawyer, Mr. Twomey, put it, if they are to join this corporation which is controlled by physicians, subscribers should be assured protection from discrimination in favor of those who are paying patients.

Article IX, Section 1, leaves the question of amendments or any changes in the by laws to a majority of the members of the corporation. The counsel for the Commissioner of Insurance asked us to change this to read "by a vote of 15 members." Our purpose is that the powers of the members cannot be altered by changes in the by laws other than those to which the members subscribe. The physicians cannot be displaced from voting membership, which gives them the powers indicated and hence, ultimately, control of the corporation.

We have presented the type of corporation embodied in the by laws to you, hoping that we have sensed the will of the majority of the Society. We ask you to consider these by laws from the viewpoint of acceptance or rejection, or from the viewpoint of modification. If your decision is that these be rejected, then we ask you to outline the type of corporation you want. We cannot proceed to the rules and regulations until the character of our corporation is determined, so that we can refer rules and regulations to some definite pattern.

We have outlined for you the pitfalls in creating a medical service corporation. We have presented a specific set of by laws that create a corporation which, we hope, will meet with your approval. In asking for action on these by laws, we suggest the necessity of committing yourselves to a specific type of corporation. In making your decision you are restricted in your choice to one of the small number of types of corporations that have appeared on the current scene. They are:

1. *Compulsory health insurance*, in which control of the corporation resides in a federal or state bureaucracy. This type of corporation we hope to avoid permanently.

2. *Lay group (nonparusan) corporation*, in which a group of disinterested laymen organizes a medical service program and, hence, controls the board of directors. It is only by their grace that a group of physicians can control the medical problems. By the same token, they can deny the physicians control over these matters.

3. *Consumer co-operative*, in which a group of non-producers controls the producers of medical service, insofar as they appoint and control the directors. As only 5 per cent of the members of a consumer's co-operative retain supervisory interest, this means that a small handful of nonproducers controls the producing group. They may delegate powers over medical matters

to a group of physicians, but they may easily withdraw this privilege, since they control the directors and, hence, the by-laws. This is a precarious basis on which to risk the security of one's self and family.

4. *Medically controlled corporation.* With proper arrangement for protection of the rights of the subscriber, this is the type of corporation to which the bulk of physicians subscribe. Control may be achieved directly by placing physicians in control of the board of directors. This has evident drawbacks, as has been indicated. The other alternative is to achieve control of the vital professional problems indirectly, as we have done, by empowering a subcommittee of physicians to initiate all action on such matters. This represents an even more complete control of these vital matters by physicians than is assured in the setup with physicians constituting a majority of the directors.

ELMER S. BAGNALL  
THOMAS H. LANMAN  
PEIRCE H. LEAVITT  
SHIELDS WARREN  
JAMES C. McCANN, *Chairman*

## APPENDIX NO. 7

### REPORT OF THE COMMITTEE ON POSTGRADUATE INSTRUCTION

Since the annual meeting, the committee has arranged a curriculum for the postgraduate extension courses for the academic year of 1941-1942; this has been sent to each district postgraduate chairman. Courses will start as soon as proper arrangements are completed.

Owing to a curtailment of governmental funds, the general courses will be financed by a registration fee of \$5.00 for each physician who takes the courses. If any district wishes a postgraduate extension course on venereal disease, this will be given free; the expense will be met jointly by governmental agencies and the Society.

The committee has co-operated with the other New England state medical societies in organizing the fourth New England Postgraduate Assembly, which will be given at Harvard University, October 29 and 30, 1941; announcement has been made in the *New England Journal of Medicine*, and programs have been mailed to all legally registered physicians in New England. Further reports on these activities will be made at subsequent meetings of the Council.

REGINALD FITZ, *Chairman*  
LEROY E. PARKINS, *Secretary*

## APPENDIX NO. 8

### REPORT OF THE COMMITTEE ON CONVALESCENT CARE

Since 1938 the Committee on Convalescent Care of the Hospital Council of Boston has been concerned with the adequacy of facilities for convalescent care and has made an investigation of private nursing homes within a reasonable radius of Boston.

On January 9, 1940, a meeting of hospital superintendents and medical social workers was called by the committee to discuss the findings in connection with visiting nursing homes and setting up the Nursing Home Information Bureau. It was found that more than 90 per cent of the patients in these nursing homes were chronic and aged, and the committee raised the question as to whether the needs of this group should not be studied. The committee was urged to turn its attention to a study of the

entire question of placement of patients in these nursing homes, both from the point of view of hospital administration and the medical social workers.

The committee therefore voted to secure a complete record of discharges from in-patient services referred to medical social service departments for aftercare for a six months' period, to obtain information as to the number of individuals involved, the types of care requested and the final disposition of each case.

The first half of the study covered the three months' period of March 18 through June 18, 1940, and the second period was from November 1, 1940, through January 31, 1941. A preliminary summary report of the findings follows. This summary report represents data presented for consideration to the Committee on Convalescent Care of the Hospital Council of Boston.

\* \* \*

### Hospitals Included in Study

One tax-supported and nineteen voluntary hospitals were asked to participate in this study and to fill out a card for each discharge referred to the medical social service department for some form of aftercare. Fifteen institutions returned cards for the study. The number of patients referred for aftercare in the individual hospitals ranged from 1 to 219. Five hospitals sent in no cards. This was due to the fact that they have no social service departments and that the hospitals were not requested to make provisions for aftercare.

### Number of Cases

It is interesting to note that there were fewer requests for aftercare during the second period of the study, that is, from November 1, 1940, through January 31, 1941, than from March 18 to June 18, 1940, the figures being 710 and 604, respectively.

### Sex, Racial, Religious and Age Incidences

One thousand three hundred and fourteen individuals were referred to the medical social service departments of the fifteen hospitals for the provision of some kind of aftercare.

Of these, 560 were males and 752 females (no report on 2); 1242 were white, 63 colored and 3 yellow (no report on 6); 453 were Protestants, 592 Catholics and 230 Jews (no report on 39); 58 were under eighteen years of age, 899 between nineteen and sixty-five and 317 were over sixty-six (no report on 40).

### Care Provided

*Own home.* Five hundred and fourteen patients returned to their homes or the homes of relatives. Of this group, 239 received care from a visiting nurse and 25 received care from a practical nurse or registered nurse or were assisted by having a special housekeeper placed in the home. Two hundred and fifty patients returned to their homes with no special nursing care.

*Institution or nursing home.* Of the total number of patients 768 had some provision made for aftercare away from home. The Committee on Convalescent Care was particularly interested in this group, the type of care required and the facilities that were used for care.

Three hundred and eighty-nine were listed as *convalescent*; 301 were between nineteen and sixty-five years of age (no report on 21). Fourteen received care in tax-supported institutions, 195 in voluntary agencies, 154 in private nursing homes and 20 in special hospitals and sanatoriums; 6 patients were listed as requiring convalescent care but no information was given as to where they were placed. Of those placed in private nursing homes, 18 stayed one week or less; 41 from one to two weeks,

43 from two to four weeks, and 28 over four weeks (no report on 24), 72 patients paid less than \$1500 a week.

Two hundred and eighty six patients required facilities for chronic care, 154 were between nineteen and sixty five years of age (no report on 13). One hundred and twelve were cared for in tax supported institutions, 30 in voluntary agencies, 122 in private nursing homes of whom 75 paid less than \$1500 a week (no report on 47) and 16 in special hospitals, there was no report on 6 patients.

Terminal care was provided for 93 patients of these 36 were between nineteen and sixty five years of age (no report on 2). Twenty one were cared for in tax supported institutions, 15 in voluntary agencies, and 47 in private nursing homes (no report on 10), 20 private patients paid less than \$1500 a week.

Thus we find that of the 768 patients for whom care was provided in an institution or nursing home, 389 or 50.7 per cent, were convalescent, 266, or 37.2 per cent were chronically ill and 93, or 12.1 per cent needed terminal care.

#### *Adequacy of Care*

A report on the adequacy of the care provided shows that in 1072 cases the arrangements made were considered satisfactory, 134 were unsatisfactory, 11 were questionable. 6 patients died before arrangements could be completed. 3 patients were still in the hospital at the time of the close of the study, and there was no report on 84 cases.

The reasons given for dissatisfaction varied. Among those listed were lack of medical supervision in the nursing home, patient needed more care than available, patient or family refused to accept recommended plan of care away from home, patient complained of care according to the Nursing Home Information Bureau, the home was not very good, but the family arranged for admission. Patient could not adapt to group care in public institution. Home conditions poor, patient emotionally restless in new group and missed frequency of doctor's attention received on ward, distance made it difficult for relatives to visit, no occupational therapy in nursing homes, atmosphere of chronic invalidism for convalescent patient.

#### *Diagnosis and Prognosis*

No attempt has been made at this time to analyze the diagnoses or prognoses of the cases referred for aftercare or to relate them to any age grouping or type of care recommended.

#### *Charges*

The hospitals were asked to indicate the amount paid for aftercare and who paid it, that is, the patient, the social service department or some other private agency. They were also asked to indicate whether the patient paid from public-relief funds. Attention is called to the fact that the privately owned nursing homes are run as a business and for this reason seldom admit a patient on a free basis, although in justice to them, it must be said that in some cases they have continued care on a free basis or for a small charge. Patients admitted to tax supported institutions are, for the most part, admitted without charge.

One hundred and nine patients were listed as receiving free care, 329 paid for their care, 189 received public funds, 132 had their care paid for in full or part by the social service department, 104 were aided by other voluntary agencies.

T DUCKETT JONES  
HENRY I. GALLUP

• • •

After nearly three years of study of the needs of convalescent patients and existing facilities for their care

it has been found that convalescent care merges into the care of the chronic patient and the latter into the problem of caring for the aged. The privately run nursing home is essentially a home for aged persons with their chronic ailments. It is not a solution to the problem of convalescent care except for patients who can pay the higher rates in the better homes.

This committee is concerned chiefly with providing new facilities for the convalescent patient discharged from the wards of hospitals belonging to the Hospital Council and from other agencies in Boston, for example, the Community Health Association.

As a result of the tabulations recently made by medical social workers, it has been found that although the problem of convalescent care is an acute one it is not so great numerically as had been anticipated. The committee is agreed that although the tabulations show that there is need for facilities for an equal number of chronic patients, who would require longer periods of care, it is the function of this committee to concentrate on a solution, first of the convalescent problem.

The committee also believes that there is more information to be secured from the study with relation to the chronic patient and that, when the convalescent question has been reasonably well solved, attention should be focused on the chronic problem. Further consideration of these problems will constitute the immediate deliberations of the committee.

T DUCKETT JONES  
HENRY I. GALLUP

#### APPENDIX NO 9

##### REPORT OF THE COMMITTEE APPOINTED TO SUPERVISE THE APPROPRIATION BY CONGRESS FOR THE CONSTRUCTION OF A NEW BUILDING TO HOUSE THE ARMY MEDICAL LIBRARY AND MUSEUM

Word has been received from the Surgeon General of the United States Army in regard to the present status of the projected Army Medical Library and Museum. Final clearance of the site has been approved by the National Capitol Park and Planning Commission. That commission and the Fine Arts Commission have approved the design of the building and its setting on the designated site. The building is to occupy a block directly across the street from the Senate Office Building and adjacent to the Library of Congress on Capitol Hill.

A bill for the purchase of the land authorizing \$1,000,000, was approved by the Bureau of the Budget, passed by the House of Representatives, approved by the Senate Military Affairs Committee and on August 15, 1941, was before the Senate itself. In addition, funds for architect's fees have already been authorized and a contract has been made with Eggers and Higgins, who are now engaged in the preparation of plans.

HENRY R. VIETS, Chairman  
ROBERT B. OSGOOD  
BENJAMIN SPICTOR

#### APPENDIX NO 10

##### REPORT OF SPECIAL COMMITTEE TO EQUALIZE DISTRIBUTION AMONG PHYSICIANS OF MEDICAL SERVICE TO WPA EMPLOYEES

Each month since our last report, a member of our committee has visited the WPA office in Boston, checked the records of payments to physicians and discussed matters relating thereto with Mr. Burns, State Compensation Of-



ficer. Very little of a controversial nature has arisen. Perhaps this is in considerable part due to the marked decrease in the number of WPA employees, with a consequent reduction in the number of those injured. In August this year the average number carried on the WPA rolls was 37,622 employees; in contrast, in 1938 the number was 126,165. The years between 1938 and 1941 show a progressively consistent decline in the number of those employed.

While on figures, an error made in the copying of our last report should be corrected. In the last paragraph of that report, it should read as follows: "\$1,047,401 has been spent for the total care of the approximately 85,000 injured workmen." This means a little more than \$12.00 for each case treated. The WPA office feels that this figure compares favorably with the amount paid for compensation cases in this commonwealth, which is approximately \$23.00.

In our last report to the Council it was stated that the State Compensation Officer and the committee planned to make \$500.00 the top at which a physician's name would be removed from the list of available physicians. An advisory letter from the Commission in Washington resulted in a change in this figure, and it was made \$1000.00 instead of \$500.00. Since about June 1, then, the \$1000.00 top has been in operation. Orders went out to all WPA timekeepers that no injured workmen be referred to any physician who had received that amount, or more, in fees from this type of work since its inception. Exception was to be allowed if the injured party specifically requested his family physician.

Under the date of May 10, 1941, a new ruling was made by the Commission in Washington. It did not come to our attention until after the meeting of the Council in May. To quote from this ruling: "In *doubtful* cases injured employees may *not* indicate their personal preferences, and shall *not* be referred to physicians of their own choice. Where federal medical facilities are not available, doubtful cases shall be referred by the project timekeeper to specially qualified physicians duly licensed under the state law to engage without limitation in the practice of medicine and surgery." The Committee did not favor this ruling, but experience had been bad with free choice according to the Commission, and we were not successful in our attempt to have it reversed. It was not deemed wise to make an issue of it, especially as it would include but a very small proportion of the cases. No complaints have been received as yet, and this rule has been in effect for several months.

With such a sharp reduction in the WPA rolls, the work of this committee should noticeably decrease. Regular formal reports to the Council may be omitted unless matters of importance arise.

GUY L. RICHARDSON, *Chairman*  
WILLIAM E. BROWNE  
LUCIEN R. CHAPUT  
DANIEL J. ELLISON  
FRANCIS P. MCCARTHY

## APPENDIX NO. 11

### REPORT OF COMMITTEE FOR STUDY OF PRACTICE OF MEDICINE

Although this committee was appointed in the spring of 1941, its assignment is no new interest of the Massachusetts Medical Society. One hundred and sixty years ago our society was chartered, among other things, to examine candidates for the practice of physic and surgery

and to grant letters testimonial of the examination of such as were found skilled in their profession. The thoroughness with which this was carried out has been recalled recently by the publication in the *Journal* of an account of the examination of John Fleet in 1788.\* There were controversies in those days, too, but they were smoothed without great difficulty, and the Society continued to protect the people against "those who may ignorantly and wickedly administer medicine" until 1894, when Massachusetts adopted its medical practice act. The story of these first hundred and twelve years is told in Chapter IX of Dr. Burrage's *History of the Massachusetts Medical Society*. It is referred to here because it establishes the fact that the Massachusetts Medical Society has traditionally upheld the highest standards of medical education and practice, and suggests that it should continue to do so.

The highest standards of medical education and practice are no longer maintained in Massachusetts. Here are the plain facts. In 1940, Massachusetts registered as many graduates of unapproved schools as did all the other states of the Union combined. In 1940, Massachusetts registered more graduates of unapproved and foreign schools (for which we have no method of approval) than she did graduates of the approved schools, including diplomates of the National Board of Medical Examiners. The data for the following tabulation are taken from the compilations of the American Medical Association:†

STATUS	MASSACHUSETTS LICENSURE FOR 1940‡				TOTAL
	APPROVED SCHOOLS	NAT. BOARD MED. EX.	UNAPPROVED SCHOOLS	FOREIGN SCHOOLS	
Examined	110	0	303	223	636
Passed	101	113	125	112	451
Failed	9 (8%)	0	178 (59%)	111 (50%)	298 (47%)

‡This tabulation has been changed from that presented to the Council on October 1 by the addition of the figures for those registered through endorsement of National Board Examinations.

This lamentable state of affairs has come about because the Massachusetts medical practice laws are geared to the nineteenth rather than to the twentieth century. The Association of American Medical Colleges and the American Medical Association have been raising the standards of medical education now for many years. As the medical schools became graded and improved, most state licensing boards began to take an interest and to co-operate in the formulation of new legal requirements that embodied the same educational ideas. Whereas only five state licensing boards refused to recognize the low-grade schools in 1904, the number of such boards had risen to forty-six by 1925. The fact that Massachusetts, in 1941, continues to recognize them means that for fifteen years we have been absorbing the country's second-rate educational output. For those who have practiced medicine for twenty years or more in any part of the Commonwealth figures are not needed to establish this fact—indeed it is a notorious fact throughout the rest of the United States that we are beginning to feel the effect of allowing our state to be the dumping ground for poorly trained physicians and surgeons.

The responsibility for this state of affairs is not easily placed. There are half a dozen things which might or might not have been done in the past, and there are a dozen reasons why they were or were not attempted. The present status is that although we are still operating under what a member of our own state board has called an "out-of-date and clumsy medical practice act," we have a State Approving Authority, which we expect will be able in 1945 to separate out and refuse the privilege of examination to graduates of medical schools that are not in its

\*Fleet, J. A fiery ordeal. *New Eng. J. Med.* 224:1006-1014, 1941.

†Medical licensure statistics for 1940. *J. A. M. A.* 116:2021, 1941.



opinion living up to the present day standards of medical education. It would seem to be idle to develop controversies now, when we are hopefully awaiting the tardy operation of this state authority, which was designed for and may yet be found to supply the necessary relief. This authority has no easy task before it. Controversies within the profession cannot help it and may supply material for political resistance to the consummation of its effort. We should support it firmly to the end that it may establish itself as completely and satisfactorily in Massachusetts as other similar authorities are already established in other states. Such support, however, need in no way deter us from an advance consideration of what our course should be if this authority is forced to succumb to opposing minorities in 1945.

If, in 1945, we find that we are merely awakening from a dream and that, in spite of our efforts and opinions, the people of Massachusetts wish to leave their backdoor open to the poorly trained physicians of the entire world, there is no reason why we should continue to pretend that the standards of the Commonwealth are sufficient for membership in our society. To do so would be contrary to the past history of this society and of all reputable medical organizations. The trial of the American Medical Association in Washington at least determined that a medical society has every right to maintain high professional standards of membership.

Those who now come into the practice of medicine through the approved channels of medical education have been highly selected, not only as to their scholastic aptitudes (which is all that any examination can cover) but on personal grounds as well. This selection beginning in college and continuing through medical school, is an expensive process, and although it does not weed out all the undesirable elements it comes as close to that accomplishment as possible. This is recognized by the Council's annual approval of the list of medical schools and colleges prepared by the Committee on Medical Education and by Chapter V, Section 2 (a) of the by-laws which provides for the admission of the graduates of these medical schools and colleges into the Society. Under Chapter V, Section 2 (b), however, the by-laws provide the machinery for admitting graduates of schools *not* recognized by the Council. The propriety of this arrangement rests on the assumption that the Society is willing to admit to fellowship graduates of schools which it is unwilling to recognize. This is a good democratic assumption but if it is allowed to operate indefinitely, it encourages the schools concerned to continue their resistance to inspection and improvement, and cannot but discourage the embryonic State Approving Authority in the initial efforts of what we have admitted is a difficult task. If we believe and want the members of the State Approving Authority to believe, that the present standards of medical education

are worthy, fair and just we should consider whether our requirements for admission to fellowship should not be as unequivocal as those of the United States Army, Navy and Public Health Service or of the National Board of Medical Examiners—not to mention most of the other states in the Union, that is, whether we have been too freely invoking Section 2 (b) under Chapter V of the by-laws.

This question is brought up now because it suggests a possible concrete step to be taken some few years hence. Consequences which might reasonably be expected to follow such a step may now be outlined. The better hospitals of Massachusetts would doubtless continue to require membership in the Massachusetts Medical Society as a qualification for staff membership. Their standards would thus be supported and gradually raised, and the medicine and surgery practiced within their walls would continue to improve. The nonconforming type of hospital on the other hand would be more conspicuously placed as an institution of lower standards. This would tend to concentrate the responsibility for the practice of good surgery even more emphatically where it already rests—in the hands of the hospitals. It is the opinion of this committee that the responsibility for the practice of surgery belongs in the hands of the hospitals, and that practical regulation can best be approached through registration or supervision of these institutions. It so happens that current legislation has been enacted charging the State Department of Public Health with responsibility for the licensing of hospitals and for setting standards for hospital equipment, records and so forth. The committee therefore recommends that the Massachusetts Medical Society heartily co-operate with the Department of Public Health in meeting this responsibility.

In summary. The standards of medical practice in the Commonwealth of Massachusetts are low. An attempt is being made in good faith to raise them through the establishment of the State Approving Authority. Controversies among those who are actively supporting this attempt are embarrassing and should be avoided. If the authority is obstructed in bringing about a higher standard of medical practice in Massachusetts, this society need no longer invoke Chapter V, Section 2 (b) of its by-laws, and may thus return to its traditional policy of supporting the highest standards of medical education and practice. This is a decision for 1944. Whether or not such a policy on the part of the Society becomes desirable at that time, an opportunity to co-operate with the State Department of Public Health in its licensing of hospitals is now at hand. The committee recommends that this opportunity be seized as an immediate step toward improving the practice of medicine and surgery within the Commonwealth.

DWIGHT O'HARA, *Chairman*

## MEDICAL PROGRESS

### METABOLIC FACTORS IN THE CAUSE AND CONTROL OF DENTAL CARIES

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BOSTON

IN 1931, Hanke<sup>1</sup> wrote, "The literature pertaining to dental pathology is a chaos of facts and fiction (the latter being the outcome of a hyper-enthusiastic championship of a fixed idea) . . . ." In 1933, Howe and his associates<sup>2</sup> stated:

In the past few years, several reports have been made of the arrest of caries through dietary changes in various children's institutions in this country and in England. The preliminary findings of a recent survey carried on at Forsyth Dental Infirmary indicate that results similar to those reported from the institutional studies may be secured by the practitioner who has a working knowledge of nutrition.

This statement and the careful work of Zilva and Wells,<sup>3</sup> Howe,<sup>4</sup> McCollum and his co-workers,<sup>5,6</sup> Höjer,<sup>7</sup> Wolbach and Howe,<sup>8</sup> Mellanby,<sup>9</sup> Boyle and his associates<sup>10-12</sup> and others on the striking specific effects of vitamins A, C and D on the teeth of experimental animals suggested that the studies of subsequent years might provide objective information that would turn the chaos in the older literature on dental caries into an orderly sequence of established and generally accepted facts.

In 1939, The American Dental Association<sup>13</sup> published a book entitled *Dental Caries: Findings and conclusions on its causes and control*. The one hundred and ninety-five summaries presented therein by observers and investigators in twenty-five countries provide a relatively up-to-date cross-section of the dental profession's opinions on the etiology of "the most prevalent of all diseases." The report deserves careful study, because it depicts dental opinion in 1939 as compiled by the American Dental Association. I believe that it can be visualized without gross misrepresentation by presenting isolated but not distorted quotations from this authoritative source.

#### DIET IN GENERAL

There is no evidence that caries is produced by malnutrition or may be prevented by adequate diets.

Dental caries arise from metabolic disturbances which can be avoided or corrected through the use of diets high in all recognized nutritional essentials.

All articles in this series will be published in book form: the current volume is *Medical Progress: Annual, 1940* (Springfield, Illinois: Charles C Thomas Company, 1941. \$4.00).

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The author has not observed any favorable results on the progress of caries from changes in diet including additions of calcium, phosphorus and vitamins.

#### "CIVILIZED DIETARY"

The ultimate causes of caries reside in refinements of civilization and resulting changes of diet. To prevent caries the diet should be "natural" and rich in vitamins and minerals.

There is no basis for the view, frequently held, that freedom from caries in a primitive people is due to nutritional superiority of "natural" as compared with "civilized" diets.

#### CARBOHYDRATE IN DIET

Sugar or starch has not been observed to favor caries, unless use of either materially diminishes the amounts of ingested protective foods.

Active caries was induced in children by increasing the sugar intake while they were receiving a diet that nutritionally was adequate.

Amount of carbohydrate in the food is not [an] important [factor], provided all essentials are included in the diet.

#### ORAL BACTERIAL FLORA

No consistent relationship has been found between . . . state of mouth hygiene and activity of caries.

The most constant differential between caries-free and caries-susceptible persons . . . is that of relative number of *L. acidophilus* organisms in the mouth.

Studies of mouth flora have shown that children, after definite arrest of extensive caries . . . , may show high counts of acid-producing bacteria, especially *B. acidophilus*.

#### COMPOSITION OF SALIVA

Chemical analysis of saliva has revealed no correlation with activity or inactivity of caries.

Three factors cause susceptibility to dental caries: . . . (3) lack of sufficient phosphate in saliva to prevent solution of teeth salts by acid under bacterial plaques.

No correlation has been demonstrated between amounts of salivary calcium, phosphorus, chlorides, pH, CO<sub>2</sub>-capacity, total alkalinity, total solids or ash and activity of caries.

#### ACID-BASE BALANCE

The extent of excess of basic over acid metabolic end-products of the diet is unimportant in relation to caries.

The two most important relationships in caries prevention are the acid/base and calcium/phosphorus balances in the body.

No relationship has been demonstrated between intake of calcium, phosphorus or acid-base dietary values and activity of caries.

## CALCIUM AND PHOSPHORUS BALANCES

Retention levels of calcium, phosphorus and nitrogen are not correlated with presence or absence of caries.

Increased retention of calcium favors caries prevention.

There is no proof that addition of milk to ordinary devitalized diet prevents or cures dental caries.

With increased Ca intake [as in milk] there is a decreased tendency to caries.

The phosphorus deficiency theory accounts for . . . caries of pregnancy.

Pregnancy does not cause caries.

## HARDNESS OR CALCIUM CONTENT OF WATER

Calcium laden drinking water does not prevent caries.

There is an inverse relationship between drinking water hardness and caries incidence [that is, hard water does prevent caries].

## VITAMINS

Caries arises independently of the amount of vitamin C in the diet.

The dietary factors of chief importance to calcified dental tissues are vitamin D and A and mineral salts.

Addition of calcium and cod liver oil . . . to the diet of a caries susceptible does not reduce the disease.

It is interesting to note that in the general analysis of the findings and conclusions of this book no mention is made of vitamin C.

Naturally, this consolidation of contradictory statements places the conflict of opinion very much in the foreground. On the other hand, the limitation of the quotations to less than one third the contradictory opinions encountered in reading the report indicates that the conflict has not been exaggerated. If the picture is distorted, it is because it includes none of the details that distinguish the controlled experimental evidence obtained by sincere investigators from the theory of pseudoscientific enthusiasts. But the book itself includes no such details in the three pages of introduction or the one hundred and seventy pages of summaries or the fifteen pages of analysis of the findings and conclusions. However, at least three summaries, perhaps best described as fantastic theoretical verbiage, are not only included but also given the importance of being referred to in the analysis of the findings and conclusions. A more recent article by Fleisch<sup>14</sup> extends the theorizing about dental caries to the significance of the vitamin B factors but fails to present any definite facts concerning the role of these substances in the cause or control of caries.

Although Mellanby's experiments on dogs led her to emphasize the importance of vitamin D, calcium and phosphorus in the proper structural development of teeth in dogs, she<sup>15</sup> remarked: "There is as yet little direct evidence of the effect of diet on tooth structure in man. . . . However, a small amount of data suggests that good structure

of the teeth in man is obtained by following the same principles of diet which result in good teeth in dogs." Toverud and Toverud,<sup>16</sup> from experiments on dogs, concluded that a diet deficient in calcium, phosphorus and vitamin D during pregnancy and lactation predisposed the offspring to rickets and dental caries. They did not hesitate to correlate enamel hypoplasia and caries. Rosebury and Foley<sup>17</sup> reported that diets deficient in calcium and vitamin D had no deleterious effect on rats during pregnancy and lactation or on their young. Boyle and Bessey<sup>11</sup> stated that the carious processes in the guinea pig do not appear to be associated with defective tooth structure or with dietary deficiencies of vitamins A and C.

Young,<sup>18</sup> from studies with Mellanby on a group of children in Birmingham, believed that there was a significant association between tooth structure and initial caries and spread of caries, and that the ingestion of vitamin D during the period of tooth development before and after tooth eruption diminished the incidence of enamel and dentin hypoplasia and caries. Previously, Hess and Abramson,<sup>19</sup> in reporting studies on a group of institutionalized children, expressed a similar opinion concerning the role of vitamin D, although they called attention to the fact that the permanent incisors, which calcified during the rachitic period, were rarely carious, whereas the second permanent molars, which calcified after the rachitic age, were frequently carious. They further expressed the belief that lack of vitamin B, C or A did not play a significant role in caries. Fish<sup>20</sup> also called attention to the lack of correlation between teeth developed during the rachitic period and teeth having caries. In a recent paper, Boyd,<sup>21</sup> although emphasizing the value of vitamin D, arrived at the following somewhat indefinite conclusion, "The child with active caries must be considered to have a disturbance of metabolism, and this can be corrected most effectively through enrichment of the diet so that it will favor an optimum state of nutrition." Hess, Lewis and Roman<sup>22</sup> and Kronfeld and Schour<sup>23</sup> demonstrated that postnatal nutrition from birth to ten years of age is usually far more important to calcification of teeth than prenatal nutrition is. On the other hand, Toverud and Toverud<sup>16</sup> made much of the effect of prenatal nutrition on the first permanent molars as well as on the deciduous teeth. However, much of their evidence was based on experiments with dogs in which the conditions were extreme. Rare cases of the effect of extreme conditions of prenatal nutrition in man are provided by the structural defects in the deciduous teeth of infants with fetal rickets.<sup>24</sup>

As an explanation of why the hope of more specific knowledge from dental studies has not been fulfilled, certain considerations seem of interest. First, experimentation in this field is recent. Prior to 1920, metabolic research was largely concerned with total energy metabolism or total maintenance requirements and, therefore, did not provide the knowledge and technics applicable to the study of dental physiology. It was only when the establishment and cure of vitamin A, C and D deficiencies in experimental animals became susceptible of accurate control ten to twenty years ago that experiments on mineral metabolism were controlled and that experiments carried out by the investigators mentioned above<sup>3-12</sup> provided accurate information on the effect of vitamins A, C and D on the growth and development of teeth in animals. Secondly, warnings by careful investigators that conclusions concerning the relatively slow-growing or static teeth of human beings could not be drawn too readily from experiments on the rapidly or constantly growing teeth of animals seem to have been ignored by many. Thirdly, the application of this experimental knowledge to the problem of human caries, as indicated by the dental literature, was undertaken largely through studies of two types. One attempted to determine the effect of particular factors on groups of relatively healthy people; in such studies, extreme enough conditions were rarely established to assure predominance of the factor in question. The other embraced surveys of racial groups living under different conditions and consuming different diets. Here, too, control of the various factors in question was extremely difficult. Finally, the tendency to separate dental from medical clinics resulted in relatively few studies on the almost ideal ready-made extreme experimental conditions provided by sick patients in medical clinics. For this or some other reason, much of the very definitive information that has resulted from observations on such patients seems to have received little emphasis. A summary of such information follows.

Albright and his co-workers,<sup>25, 26</sup> Stafne and Austin<sup>27</sup> and Strock<sup>28</sup> have amply demonstrated that patients suffering from the extreme skeletal demineralization of hyperparathyroidism usually show no demineralization of the teeth or increased caries, although isolated cases of caries in such patients may be observed.<sup>29</sup> Maxwell and Miles<sup>30</sup> noted that severe osteomalacia in Chinese women did not result in caries, even though the teeth might fall out. Taylor and Day<sup>31</sup> likewise observed that women in the district of Punjab, India, — suffering from deficient diets, frequent pregnancies, long-continued breast feedings, chronic osteomalacia, tetany and deformities — usually had

nearly perfect teeth. Smyth and Goldman<sup>32</sup> observed good teeth in a fourteen-year-old boy with renal insufficiency who had suffered for over a year from the skeletal demineralization of renal rickets. At the Children's Hospital, good teeth have been observed in patients who have had renal rickets for a year or more and who at the time of examination were shown to have marked acidosis, low serum calcium, marked resorption of the supporting alveolar bone, absent lamina dura and generalized skeletal demineralization. Whether the demineralization in these renal cases resulted from the chronic acidosis or the secondary hyperparathyroidism is of no concern. But the fact that patients with chronic renal disease, osteomalacia or osteitis fibrosa generalisata can have extreme skeletal demineralization that does not affect the teeth suggests how little likelihood there is that the teeth are affected by such minor alterations in calcium and phosphorus or acid-base balances as those produced in the group type of experiments on relatively healthy persons.

As early as 1906, Erdheim<sup>33</sup> noted in rats that layers of dentin laid down while the rat was in the hypoparathyroid state failed to be calcified. Albright and Erdheim, in unpublished experiments, later showed that this acalcification of the dentin could be rectified by the injection of parathyroid extract into the rats. Albright and Strock<sup>34</sup> observed that the teeth of children who had developed hypoparathyroidism during adolescence failed to mature after the time of the onset of the disease. The experimental work from the laboratories of Schour<sup>35</sup> and Ziskin<sup>36</sup> confirms these findings. The delayed eruption and maturation of teeth in cretinism is well known. Ziskin and Applebaum,<sup>37</sup> in studying thyroidectomized rhesus monkeys observed both a delay in rate of dentin growth and an alteration in the quality of dentin calcification. Rony<sup>38</sup> reported marked delay in the shedding of deciduous teeth and in the eruption of permanent teeth in a patient with hypopituitarism. The marked rarefaction and fibrosis of alveolar bone with disappearance of lamina dura, resorption of tooth roots and hypercementosis that may occur in Paget's disease do not result in caries.<sup>27, 39-41</sup>

The foregoing evidence for the stability of the structure of the adult tooth in the presence of metabolic disturbances suggests, in spite of the popular belief to the contrary, that the drain on the calcium and phosphorus stores during pregnancy and lactation does not result in the demineralization of the teeth of women at such times. Eaton<sup>42</sup> concluded that any increase in caries during pregnancy was due to laxity in oral

care and not to pregnancy per se Ziskin and Hotelling<sup>43</sup> stated that "pregnancy is not a cause of dental caries" and that "some factors operating during pregnancy actually prevent tooth decay to a significant extent" Weisberger,<sup>44</sup> in studying a larger group of women during pregnancy and lactation at the Boston Lying in Hospital and Harvard Dental School, did not observe any increased incidence of caries Ziskin, Blackberg and Stout<sup>45</sup> described a gingivitis during pregnancy characterized by an epithelial hyperplasia that may well have been associated with some endocrine disturbance accompanying pregnancy Ziskin<sup>46, 47</sup> has discussed the possible role of endocrine disturbances in hypertrophic and desquamative gingival conditions not associated with pregnancy. His implications concerning the beneficial effects of hormonal therapy need confirmation and obviously may not be applicable during pregnancy

Bloch,<sup>48</sup> after studying the teeth of children who had manifest signs of vitamin A deficiency in infancy, concluded "In man, deficiency in vitamin A has no specific injurious effect on the formation and calcification of the teeth A disposition to dental caries, therefore, cannot be due to deficiency in vitamin A in infancy" Hess and Abramson<sup>14</sup> expressed a similar opinion Boyle<sup>49</sup> examined the tooth germ of a three and a half month old infant who by post mortem examination was found to have congenital syphilis and the generalized epithelial changes of vitamin A deficiency Ruling out the effects of syphilis, Boyle concluded that vitamin A deficiency may result in a hypoplasia characterized by atrophy of the enamel organ, with replacement of the enamel-forming cells by squamous epithelium and cessation of enamel formation and by defectively calcified dentin

Westin,<sup>50</sup> from studies of the scorbutic changes in the teeth and jaws of man, concluded that, although such changes were analogous to those in the guinea pig, none of his findings indicated that scurvy had any decisive effect on the formation of dental caries All his adult men with scurvy were practically free of caries Hess and Abramson<sup>19</sup> reported the same experience with children who had had infantile scurvy Boyle<sup>1</sup> studied the germs of the permanent and deciduous teeth in two cases of acute scurvy in infants eight and eleven months of age Each tooth germ was essentially normal Such minor changes as were found in several tooth germs of the younger child were in marked contrast to the striking lesions in the constantly growing incisors of scorbutic guinea pigs In a later paper, Boyle<sup>10</sup> remarked that, "from the evidence at

present available, dental caries in man and in the guinea pig does not appear to be due to a deficiency of ascorbic acid in the diet" He also stated that the clinical reports of Aschoff and Koch<sup>52</sup> and of Westin<sup>53</sup> suggest an immunity rather than a susceptibility to caries in ascorbic acid deficiency Crandon, Lund and Dill,<sup>54</sup> in their excellent study of acute experimental human scurvy, observed no changes in the teeth of a person who had been on an ascorbic acid free diet for six months and had definite manifestations of scurvy They did, however, observe a small hemorrhage at one gingival margin and interruptions of the lamina dura as visualized in roentgenograms Boyle, Bessey and Wolbach<sup>55</sup> observed in human beings on diets deficient in ascorbic acid a diffuse alveolar bone atrophy type of periodontal disease similar to the changes that Gottlieb<sup>56</sup> described in pyorrhea Howe<sup>4</sup> had previously noted that the dental effect of scorbutic diets on guinea pigs "more closely simulates pyorrhea than does any such condition produced experimentally"

Eliot, Souther, Anderson and Arnim,<sup>57</sup> in a study of children known to have had infantile rickets, observed a definite direct relation between hypoplastic defects of the enamel of permanent teeth and rickets but only a questionable relation between caries and rickets Hess and Abramson<sup>19</sup> reported a higher incidence of caries in a small group of children who had had rickets than in a control group On the other hand, they observed that a group of colored children who had had rickets had a lower incidence than white children with no ricketic history Shelling and Anderson<sup>58</sup> found that the incidence of dental caries in the deciduous teeth of a group of children who had had rickets during infancy was not greater than that of those who had been given vitamin D and had not had rickets Enamel hypoplasia was found oftener in the deciduous and permanent teeth of the post-ricketic group They concluded that their findings did not indicate a protective effect of vitamin D against caries in deciduous teeth or a relation between rickets and dental caries or between hypoplasia and caries Taylor and Day<sup>9</sup> found that children born of mothers with osteomalacia and reared on diets deficient in calcium and phosphorus and with a past history of infantile rickets had teeth with little or no hypoplasia or caries However, Toverud and Toverud<sup>16</sup> and Wolfe<sup>4</sup> have shown that gross hypoplasia of deciduous teeth may occur in such children Hjarne<sup>60</sup> reported a high incidence of hypoplasia in children who had had infantile tetany Rony<sup>38</sup> has suggested that the

presence of hypoplasia following rickets depends on the persistence of a low serum calcium concentration at some time during the period of tooth development. Hess and Abramson<sup>19</sup> expressed a similar opinion. Experience at the Children's Hospital with a group of children suffering from resistant rickets suggests a correlation between the degree of hypoplasia and caries and the past history of tetany and poor skeletal mineralization during the period of tooth maturation. Similarly, a child who, following the removal of a large section of small intestine, suffered from the age of two to six years with diarrhea, poor skeletal mineralization and tetany had marked hypoplasia and caries. Albright and Strock's<sup>24</sup> observation that the hypocalcemia of children with hyperparathyroidism affected the calcification of teeth indicates that in the absence of osteoporosis a low serum calcium concentration may result in faulty development of teeth. Because studies of teeth in hypoparathyroid tetany have dealt with patients older than those with infantile tetany, involvement of the crowns of the teeth to any great extent has not been noted.

Thus, in spite of the persistence of contradictions concerning the cause and control of dental caries in man, the experimental evidence and the clinical findings suggest the following:

Dietary deficiencies at the period when teeth are being laid down may cause hypoplastic defects in infancy and childhood that persist thereafter. The slow growth and prolonged period of calcification of human teeth renders them less susceptible to periodic deficiencies and metabolic disturbances than the rapidly growing teeth of experimental animals. Static, fully developed human teeth are practically immune to demineralization, whereas the constantly growing teeth of animals remain vulnerable to metabolic defects. Much of the contradiction in the literature on dental caries in man derives from unwarranted deductions from animal experiments and from the fact that many studies on man have involved experiments that, in the light of present knowledge, could hardly yield other than inconclusive results. The relation between enamel hypoplasia and dental caries needs further definition. No specific dietary factor or metabolic condition has been proved to cause or control dental caries in the fully developed human tooth.

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 27451

#### PRESENTATION OF CASE

A sixty-eight-year-old housewife was admitted to the hospital because of vomiting and diarrhea.

She was apparently in good health until about seven weeks before entry, when she was seized with cramping pains in the left lower abdomen, associated with distention. After a short time, she began to have from six to eight watery, mucoid, blood-free stools a day. She also had spells of vomiting, always preceded by nausea. The vomitus was copious, fluid, green and free of blood. The combined attacks of abdominal cramps, diarrhea, distention, nausea and vomiting tended to be intermittent, with periods of constipation and freedom from pain, nausea and vomiting. After several weeks, there appeared a constant, gnawing pain in the left upper quadrant of the abdomen, which was relieved by morphine given by a local physician. According to the patient, this medication precipitated headaches and visual disturbances, which accompanied her acute episodes of cramps and vomiting. Her appetite became poor, and during the illness she lost about 45 pounds in weight. She became progressively weaker, until she was unable to walk across a room without support. In addition, there was a feeling that food would occasionally stick in her throat, approximately at the level of the junction of neck and chest. There was also cough, productive of yellow, mucopurulent sputum. At no time in the illness was there chest pain, hemoptysis or jaundice. Two weeks before entry, a physician removed a rectal polyp.

The patient had long experienced nocturia. Four years before her last illness, she felt weak and was treated medically in a local hospital, with a diagnosis of "Bright's disease." The family history was not significant.

Two days before admission, the patient entered another hospital, where she was found to be chronically ill and wasted. The eyes were sunken, and there was a scaling, red eruption over the nose and malar prominences. The skin was generally loose and flabby, and there was pitting edema over the sacrum and in both ankles. There was a

small nodule in the thyroid gland, both lobes of which were palpable. The chest showed increased resonance and fremitus over the right apex posteriorly, with many coarse rales in this area, and a few scattered rales over both bases. The heart was not remarkable. The spleen and liver were not palpable. There was some fullness over the lower abdomen, with an irregular mass in the suprapubic region, extending to the left lower quadrant, where there was local tenderness. The mass was palpable rectally, but there were no nodules within the rectum itself, and sigmoidoscopic examination was negative. On pelvic examination, the entire pelvis felt "frozen," and the uterus seemed connected with the suprapubic mass. The vagina was atrophic, admitting but one finger. The superficial lymph nodes were palpable. The blood pressure was 120 systolic, 80 diastolic.

The temperature was 98.6°F., the pulse 104, and the respirations 24.

Examination of the blood showed a red-cell count of 4,860,000 with 92 per cent hemoglobin, and a white-cell count of 13,750 with 72 per cent mature polymorphonuclears, 6.5 per cent band cells, 2 per cent eosinophils, 0.5 per cent basophils, 8.5 per cent monocytes and 5.5 per cent myelocytes. The serum albumin was 2.8 gm. and the serum globulin 2.6 gm. per 100 cc. The chlorides were 91.8 milliequiv. per liter. The nonprotein nitrogen was 54 mg. per 100 cc. The blood Hinton, Wassermann and Kahn reactions were negative.

The urine showed a ++ test for albumin and a + test for urobilinogen (no urobilin), and the sediment included large round cells, hyaline and granular casts, and 25 to 50 white cells per high-power field.

Stool examination showed positive guaiac and benzidine reactions. Gastric analysis showed 60 units of free acid following histamine. The stomach contents were free of acid-fast bacilli.

A roentgenogram of the chest showed diffuse mottling, most marked at the right base and in the right upper lobe. A flat roentgenogram of the abdomen showed numerous gas-filled loops having the pattern of small intestines. A barium enema passed through the rectum into a slightly elongated sigmoidal loop, the proximal portion of which was definitely narrowed over a distance of 8 cm. adjoining the junction of the sigmoid and descending colon. The contour of the stenosis could not be made out in any detail because of technical difficulties.

While in the other hospital, the patient ran a fever up to 101°F. rectally. Following an unsuccessful attempt to pass a Miller-Abbott tube, she was placed on Wangensteen drainage, and was



given intravenous glucose and salt solution. On the fifth day after admission, she was transferred to this hospital for operation.

Examination at this time was essentially as before. There were no significant changes in laboratory studies except for a rise in the white cell count to 21,100 with 81 per cent polymorphonuclears. Roentgenologic studies were as before, with the additional findings of generalized decalcification of the skeleton, the fracture of a mid dorsal vertebra and small amounts of fluid in both pleural cavities.

The patient was considered too poor a risk for operative intervention. She was continued on the Miller-Abbott tube. On the sixth hospital day, her temperature rose to 101°F, and she rapidly became weaker. Death occurred eight days after admission.

### DIFFERENTIAL DIAGNOSIS

DR ARTHUR W. ALLEN: Are the x-ray films here?

DR JAMES R. LINGLEY: This is evidently the area of narrowing referred to in the sigmoid. The small bowel contains much gas and is moderately dilated, but there is surprisingly little dilatation of the colon above the point of partial obstruction. The chest shows fluid in both pleural cavities and a process in the right upper lobe, the nature of which is not definite from the one film available. It could be an acute pneumonia or a chronic tuberculous infection.

DR ALLEN: The films add nothing to the report. We do see distended loops of small bowel, which means that whatever the cause the patient had intestinal obstruction. If we are to believe this story as it is written, this woman was in comparatively good health until a short time prior to her death. The seven weeks' duration prior to entry and the eight days here in the hospital give her a total illness of less than two months. We are told that during this time she lost 45 pounds in weight, a clear indication that during her present illness she could not have absorbed much nourishment.

The conditions that could produce such a picture as this are numerous. One has to think first of all of some kind of acute inflammatory process as an origin of her difficulty. The possibility of appendicitis has to be considered because that could produce a picture not too different from this with a final mass in the pelvis, with some fixation of the pelvic organs, subsequent obstruction, which might be intermittent, and finally death. Diverticulitis arising from the sigmoid could be another inflammatory cause for such a

picture, but I believe that one would see diverticula in the sigmoid if that had to be seriously considered. The question of Meckel's diverticulum has to be borne in mind, but it is not so commonly met in people of this age as in younger patients. Most of the cases of Meckel's diverticulum that have been operated on in this hospital in adults have had a preoperative diagnosis of intestinal obstruction, with a fairly long history of illness.

Then we come to the other group of diseases that must be seriously considered in a patient of this age, regardless of her well being prior to this present illness—namely, some form of malignant neoplasm. Many facts associated with this particular history and physical examination point toward neoplasm. It is perfectly possible to have had a slowly developing malignant tumor that might quite suddenly produce intestinal obstruction. The fact that the point of intestinal obstruction did not appear actually to be in this narrow sigmoid but somewhere in the small bowel does not mean that the primary disease could not have arisen from this region. The fact that a rectal polyp had been removed two weeks prior to entry makes us seriously consider the possibility of carcinoma of the rectosigmoid, perhaps developing from a polyp, which had worked its way through the bowel wall and produced a mass such as that described. One very significant point is against this possibility: the record states quite clearly that the stools were grossly blood free. They did find a positive benzidine and guaiac test in the laboratory, but carcinoma of the colon arising from a polyp will nearly always produce gross blood. That is a point we have to take into consideration in the differential diagnosis of this particular patient. Another possibility is an ovarian carcinoma that had remained localized for quite a long time and then got out of bounds, producing pressure on the sigmoid or, more likely, a loop of small bowel becoming adherent to the ovarian tumor. The story is quite compatible with such a condition. The spontaneous fracture of the dorsal vertebra is not clear to me, whether it is there or not, I cannot tell.

DR LINGLEY: I do not see it on these films.

DR ALLEN: If present, it would make one think of widespread metastases to the bones, which do rarely occur with cancer of the bowel and a little more often with cancer of the ovary, but are much less common in these two forms of malignant disease than they are with carcinoma of the breast or prostate. The marked decalcification bothers me a little although I think we see that not infrequently in elderly people. There is nothing

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## CASE 27452

## PRESENTATION OF CASE

A sixty-year-old man was admitted to the hospital because of lower abdominal pain.

He had always been in fairly good health, except for a chronic "bronchitis," gradually increasing deafness extending over a period of many years and an old "rupture." This hernia had been present for a long time in the right inguinal region and had always been reducible, although occasionally with some difficulty. A truss had been worn, and had given good support.

Three days before entry, the patient noticed slight discomfort in his lower abdomen near the hernia, characterized by a feeling of 'gas.' He paid little attention to his condition at that time, but the next day, when actual pain appeared (localized in the region of the hernia and extending across the lower abdomen), he took a dose of soda bicarbonate and Epsom salts. Following this, his pain increased. Only a scanty bowel movement was produced; the stool contained no blood. During the day, the patient experienced a questionable chill. There was no nausea or vomiting. Late in the third day, he called a physician because his pain had become too great to bear. He was given morphine, and referred to the hospital.

On examination, the patient appeared well controlled by sedation. He was an obese man, with some cough and with wheezing respirations. Loud, coarse rhonchi were heard throughout both lung fields, without other signs. The heart was slightly enlarged toward the left. The abdomen was quite obese. Tenderness and spasm were present in both lower quadrants, especially in the left, where there was some question of a palpable mass. Peristalsis was active. Two hernias were present, one at the umbilicus about 4 cm. in diameter and one extending across the right inguinal region to the scrotum about 12 cm in diameter. Both were reducible. Slight scrotal edema was present. The blood pressure was 120 systolic, 75 diastolic.

The temperature was 102°F, the pulse was 120 and the respirations were 24.

Examination of the blood showed a white cell count of 20,400 with 90 per cent polymorphonuclears, and a red cell count of 4,240,000 with 98 gm hemoglobin. The blood Hinton reaction was negative. The urine showed a ++ test for albumin, with occasional granular casts and white cells in the sediment.

The patient was at once started on sulfapyridine, and a blood level of 3 to 4 mg per 100 cc was maintained. A Miller-Abbott tube was passed. The temperature dropped to 99°F in three days,

and there was definite improvement in his condition. A roentgenogram of the abdomen, taken on the second hospital day, showed a large amount of gas in the stomach and in at least two loops of the small bowel. The tip of the Miller-Abbott tube lay in the pylorus. An ovoid area of increased density, suggesting a stone, was present in the region of the gall bladder.

The extremities became cold and sweaty, and the pulse and temperature rose sharply to 160 and 103°F, respectively. The patient thrashed about in bed, complaining bitterly of lower abdominal pain and voiding incontinently. His abdomen was more distended and firmer than it had been heretofore; peristalsis was absent. The patient was finally brought under sedation. In the next two days there was again considerable improvement in his condition, with a corresponding fall in the temperature and pulse. On the eleventh hospital day, following blood transfusion, the lower abdomen was opened under local anesthesia, by an incision splitting the right rectus muscle. The omentum was found adherent in the pelvis, covering a pocket of pus. Several similar pockets lying between loops of the small intestine were also evacuated. A Witzel enterostomy was made in the left lower quadrant, and the wound closed with drainage. The following day (thirteenth hospital day) respirations became increasingly stertorous and failed.

## DIFFERENTIAL DIAGNOSIS

DR CHAMP LYONS. This patient had a hernia for many years that gave no trouble and was easily reducible. Apparently, it was well controlled by a truss. He entered the hospital after three days of lower abdominal pain, which I interpret as gas pains, although there is no definite statement of their character in the record. Such a lower abdominal crampy pain suggests large bowel obstruction. Two days before entry, the patient took a purgative, which failed to give complete evacuation of the large bowel and increased the pain. I again believe that signifies some degree of large-bowel obstruction. The suggestive chill, the elevation of temperature and the white-cell count consistent with suppurative inflammation all make me think that the large bowel obstruction was associated with some pelvic inflammation. It is significant that there had been no nausea or vomiting such as would be more likely to occur with small bowel than with large bowel obstruction. The pain was so severe as to require morphine; this also suggests a peristaltic type of pain.

May we see the x-ray films? I should particularly like to have Dr Lingley point out the

gas in the large and small bowel and discuss its significance.

DR. JAMES R. LINGLEY: Here is the large area of calcification in the region of the gall bladder. It is quite characteristic of and undoubtedly is a stone. Here is the loop of dilated intestine that is described. It is often very difficult by x-ray study to determine whether such a loop is colon or small bowel, particularly when there is marked dilatation. In this case, I think you can see evidence of the valvulae conniventes of the jejunum rather than the haustral markings of the colon. I should be inclined to think it was small rather than large bowel, even though it is in the region of the transverse colon. No definite masses are visible, although these films were taken with a portable machine and therefore are not of very good quality.

DR. LYONS: The physical examination of the abdomen was of particular interest. There is no note of whether or not the abdomen was distended. The record simply says it was obese. The patient had active peristalsis, again a suggestion of intestinal obstruction rather than a distention of the bowel from ileus or peritonitis. The evidence of inflammation is confined chiefly to the lower abdomen, where there were tenderness and spasm and a questionable mass on the left side. The hernia was still reducible, and evidently there was no incarceration or strangulation. Scrotal edema without edema elsewhere in a man up and about again suggests to me an inflammatory infiltrative process rather than edema on the basis of cardiac failure or low serum protein. The single urine report of a ++ test for albumin, with casts, is inadequate for evaluation of the kidney function. The patient had inflammation and fever on entry, and it might be the albuminuria of the febrile reaction. No blood chemical findings were reported. The failure of the Miller-Abbott tube to pass does not disturb me because it often fails to pass in sick patients. They cannot be taken down to the X-ray Department, where one can manipulate the tube. The gallstone was in the usual position. I rather think we need not consider gallstone ileus because of the lack of symptoms of upper intestinal obstruction. The temperature dropped to 99°F. under bed rest, a consequence presumably of sulfapyridine therapy, which suggests a slow subsidence of the intra-abdominal infection. The acute collapse on the third day of hospitalization is to my mind associated with acute rupture of an abscess or of bowel, with a spread of this inflammatory process in the abdomen. From then on, the symptoms are those of peritonitis. The operative interference appar-

ently did not add much diagnostic information, and enterostomy was done, with decompression of the small bowel.

I shall confine my discussion to those diseases that I think might result in obstruction in the large bowel or arise from inflammation in the region of the large bowel.

Appendicitis with abscess formation one should consider foremost and primarily, but there was too little evidence of associated small-bowel obstruction to make appendicitis a likely possibility. In appendiceal inflammation, obstruction is much more apt to involve small bowel than large bowel. There is too little in the way of a mass to account for the acute illness. Had this been an appendicitis progressing to abscess formation making him as sick as he was, I should think that the patient would have had more of a mass in the abdomen. If this had been acute rupture of an appendix, the symptoms would have been those of peritonitis rather than of large-bowel obstruction.

Carcinoma with secondary perforation must be seriously considered. The lesions of the rectosigmoid are much more apt to give obstruction than to perforate. Perforation of neoplasms of the colon occurs most frequently in lesions above the rectosigmoid.

To my mind, the best diagnosis is diverticulitis. I am a little disturbed about that diagnosis because there was not a sufficient history of previous difficulty. There was no blood in the stool, which might suggest that diverticulitis and carcinoma coexisted. On the other hand, the story of lower abdominal inflammation, with subsequent perforation, does stand out. We must also consider obstruction. Inflammatory diverticulitis may obstruct, but this was rather an acute obstruction for the slowly developing inflammation of a diverticulitis and it is unusual for simple diverticulitis to give generalized peritonitis. Fish-bone or chicken-bone perforation of the diverticulum can produce such a peritonitis, but we have no evidence that that occurred. I believe that this man had diverticulosis for a considerable time, that he then developed large-bowel obstruction distal to the diverticulosis, and that diverticulitis followed as a consequence of this obstruction.

My final diagnoses include umbilical and scrotal hernia, cholelithiasis and diffuse peritonitis, which I believe was the primary cause of death. I think he had diverticulitis with abscess formation and subsequent rupture of the abscess, and I rather suspect there was an obstructing rectosigmoid carcinoma.

DR. ROBERT LINTON: When the record says that the patient was quite obese it is much to the point.

He was so obese that one could not tell whether he was distended or not. He was extremely difficult to handle. When I first saw him, the pain was entirely in the scrotal hernia on the right side. It stayed there for a day and then shifted to the left lower quadrant and subsequently shifted back to the right lower quadrant. The differential diagnosis while the patient was in the hospital lay between appendicitis and diverticulitis, with rupture of either one of them, and as time elapsed the diagnosis seemed to become more obvious. We thought he had diverticulitis, with rupture and abscess formation. The patient was never in any condition to make it possible to perform a laparotomy to relieve him of his trouble. The enterostomy that was made just before death was done chiefly because the Miller-Abbott tube could not be passed, and it was thought that decompression of the small bowel might help him, although little hope of saving him was entertained at that time. The clinical diagnosis, I think, on the record was diverticulitis, with abscess formation and peritonitis.

#### CLINICAL DIAGNOSES

Acute diverticulitis with rupture.  
Acute peritonitis.  
Bronchopneumonia.

#### DR. LYONS'S DIAGNOSES

Diverticulitis, with abscess formation and rupture.

Rectosigmoid carcinoma?  
General peritonitis.  
Umbilical and inguinal hernias.  
Cholelithiasis.

#### ANATOMICAL DIAGNOSES

Carcinoma of sigmoid.  
Perforation of sigmoid.  
General peritonitis, acute.  
Diverticulosis of colon.  
Polyps of sigmoid.  
Umbilical hernia.  
Inguinal hernia, right.  
Operative wound; ileostomy.

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This patient had diverticulosis of the colon, polyps and carcinoma. The carcinoma was an annular affair, which produced very severe obstruction. We found a perforation of the bowel 13 or 14 cm. back from the cancer. It appeared to be a spontaneous rupture of the intestine, possibly at the site of a diverticulum, although we could not determine that with any certainty. There was no local inflammatory process, although, of course, there was a generalized peritonitis. We could not make out evidence of successive stages of peritoneal inflammation. There was a very large gallstone, but nothing else of clinical significance.

peritoneal involvement and, probably, rupture, and indicate laparotomy. There is no evidence in the record that a vaginal examination was made. If it had been, tenderness, if not a distinct mass, would undoubtedly have been recognized in one vault or the other, and early laparotomy would have prevented this obstetric disaster. No matter how lenient one may be in attempting to place responsibility for this particular fatality, mistaken diagnosis seems to be the only cause of death.

## DEATHS

**JOHNSON**—ELMON R. JOHNSON, M.D., of Quincy, died October 30. He was in his seventy-first year.

Born in Hancock, Dr. Johnson received his degree from Boston University School of Medicine in 1895. He had been a member of the staff of the Quincy City Hospital. He was a fellow of the American College of Surgeons, the Massachusetts Medical Society and the American Medical Association.

He is survived by his widow, three daughters, two sons and two brothers.

**LEONARD**—JOHN M. LEONARD, M.D., of Fall River, died October 26. He was in his sixty-sixth year.

A native of Fall River, Dr. Leonard received his degree from the College of Physicians and Surgeons of Baltimore in 1900. He was a fellow of the Massachusetts Medical Society and the American Medical Association. He had been president of the staff of St. Anne's Hospital, Worcester, since 1937, and medical inspector of public schools for thirty-three years.

His widow, a daughter and three sons survive him.

**MACDONALD**—FREDERICK C. MACDONALD, M.D., of Boston, died October 27. He was in his sixty-sixth year.

Dr. MacDonald received his degree from Tufts College Medical School in 1901. He was a member of the Massachusetts Medical Society and the American Medical Association.

**VICKERY**—LUCIA F. VICKERY, M.D., of Jamaica Plain, died October 23. She was in her eighty-second year.

Born in Portland, Maine, Dr. Vickery received her degree from the Woman's Medical College of the New York Infirmary for Women and Children in 1892. She was a member of the Massachusetts Medical Society and the American Medical Association.

## CORRESPONDENCE

### POSTOPERATIVE RADIUM THERAPY

*To the Editor:* In the article, "Carcinoma of the Endometrium," by Dr. G. V. Smith, appearing in the October 16 issue of the *Journal*, the author concludes, "Preoperative and postoperative application of radium and x-radiation are considered valuable and probably necessary adjuncts to the best management of endometrial cancer."

Experience with the vaginal application of a 100-mg. bomb of radium to the cervical area, following total or supra-vaginal hysterectomy, was cited. An effective dosage of at least 2400 mg. hr., and at most 6000 mg. hr. in two applications within eight weeks of each other, was given.

The purpose of this letter is to inject a strong word of caution in the use of radium against the cervical stump or the site of the removed cervix, following total hysterectomy. It must be remembered that since the uterus has been removed, the pelvic viscera, namely, the small and large intestines, lie very close to the cervical stump or the area of the removed cervix. Hence, the intestine itself may be exposed to a large portion of the radium dosage given. This may result in various degrees of radionecrosis, manifested by diarrhea and cramps and later by intestinal obstruction due to adhesions or by perforation, peritonitis or the early development of an intestinovaginal fistula.

There is no effective way of screening the intestines when applying radium after hysterectomy, whether this be total or subtotal. This possible hazard should be kept constantly in mind. It looms large as a pitfall only in the hands of the occasional user of radium.

HOLLIS L. ALBRIGHT, M.D.

412 Beacon Street  
Boston

\* \* \*

The above letter was referred to Dr. Smith, whose reply was as follows:

*To the Editor:* Dr. Albright misquotes the last paragraph of my "Summary and Conclusions," which begins "Preoperative or postoperative," not "Preoperative and postoperative." Five times in the paper I refer to the use of radium before or after operation. We do not apply radium before and after operation, except in rare cases.

Concerning the cases covered in the review, namely, through 1935, the postoperative dosage of radium and screening are accurately described in the paragraph on "Postoperative radiation." The largest postoperative dose was 3000 mg. hr. In the following paragraph, I should have stated that our postoperative doses since 1935, although at least 2400 mg. hr., have never exceeded 3000 mg. hr. With the screening described, namely, 1.0 mm. of brass and 2.0 mm. of lead in addition to the 0.5-mm. silver capsule containing the radium, this dose has been found safe, as attested by the absence of complications in those so treated and carefully followed since 1935. Concerning this same paragraph, Dr. Albright makes a misstatement to the effect that a dosage of at most 6000 mg. hr. was given following hysterectomy. Actually the sentence reads, ". . . at least 2400 mg. hr. postoperatively, and two applications two to eight weeks apart, totaling 4800 to 6000 mg. hr., for those not operated on." Only patients *not* operated on receive the large doses, and these, too, are heavily screened.

At the Free Hospital for Women, where we treat approximately 150 new cases of cancer yearly and follow 300 to 400 treated cases during each year, all the possible hazards of irradiation are of necessity constantly in our minds in connection with the type and extent of the disease, the condition of the patient and operative procedures. To those of us who are using radium on an average of two to three times a week, the possible hazards loom large as pitfalls, which we must be on the alert to avoid if we can and which we often are forced to accept in situations where the likely advantages appear to outweigh the con-

ceivable disadvantages. Although we use radium often and despite our best judgment, unpredictable and unavoidable complications do develop. Therefore I take exception to Dr Albright's statement that the possible hazard of applying radium after hysterectomy looms large as a pitfall only in the hands of the occasional user, although we happen to have been fortunate in the results of our postoperative applications.

I heartily endorse his words of caution but point out that the lethal and disabling complications of carefully planned radiation are relatively rare and that considerable risk is warranted when one is aiming to render patients free of cancer.

GEORGE V SMITH, MD

Free Hospital for Women  
Brookline, Massachusetts

### ACCIDENTAL MALARIAL INFECTION

To the Editor: In a recent paper in *Venerical Disease Information* (22:271-276, 1941), concerning the technique of induced malaria used in the South Carolina State Hospital, the special point is made that patients undergoing malarial therapy should be kept isolated in a screened ward. The authors remark that some of the malarial strains examined by them and supposed to be free of gametocytes were, in fact, no different from other strains and were potentially dangerous because of the presence of these gametocytes and hence the possibility of transfer from patient to patient by certain species of mosquitoes. They also refer to reports from Europe of outbreaks of malaria because anopheline mosquitoes easily came in contact with patients undergoing malarial therapy.

It might be thought that especial attention need be given these points in the northern part of the United States, but this is apparently not so. A superficial study of an accidentally contracted unexplained case of malaria in a Boston hospital in 1940 brought out some interesting facts. The subject was a house officer whose duties included malarial treatment. While in the hospital during the winter of 1940 he was bitten several times by mosquitoes which were not identified. Within a reasonable incubation period (four to five weeks) from the date he was bitten he came down with tertian malaria. During that period he had injected malarial blood into several patients without known untoward accident. The last injection was given by him eleven days before he himself became ill. Fourteen days before he became ill he gave a 500-cc transfusion to a patient who had never had malaria and who had never been outside Massachusetts. This patient did not develop malaria. Malariaologists pointed out that the failure of the recipient to contract malaria probably but not certainly excluded the existence of malarial infection in the house officer at the time of the transfusion. Since the house officer was a reasonably careful worker, had no skin abrasions and recalled nothing unusual about the injections of malarial blood he had given to ward patients, the way in which he contracted malaria is not evident.

Stained slides of the blood of patients on his ward inoculated with tertian malaria were examined by parasitologists at the Harvard Medical School. Despite the fact that the strain of malaria used at this hospital had been circulated from patient to patient for some fifteen years gametocytes were easily found on these slides. A careful search for mosquito breeding places was planned but was

quite unnecessary. Within five minutes from the start of the search, a possible breeding place, a large shallow pool (10 by 20 feet) of water about some boilers, was found. Many adult mosquitoes were flying around in March and the men working in the boiler room said the mosquitoes had bitten them all through the winter. Several hundred larvae from this pool and a smaller number of adult mosquitoes were examined, but all were found to belong to the *Culex* genus, which, of course, has never been incriminated as a carrier of malaria. A recent survey in Suffolk County revealed that anopheline mosquitoes are occasionally present there in the summertime, and it is possible that a breeding place harboring this genus might have been found if a more thorough search had been made.

In any event it is apparent that, with the presence of gametocytes in the blood of patients undergoing malarial therapy, extreme care should be taken to avoid accidental infection.

GEORGE SASLOW

Worcester State Hospital  
Worcester, Massachusetts

### BOOK REVIEW

*In Search of Complications: An autobiography*. By Eugene de Savitsch, MD. Foreword by Arthur Krock. 8°, cloth. 396 pp. New York: Simon and Schuster, 1940. \$3.00.

This is another in the seemingly endless list of medical autobiographies and memoirs that the last few years have produced. Dr de Savitsch is a Russian whose life has been spent in his own country and Japan and the United States where he studied medicine and where he practices. He has had some lively adventures, which he narrates with a certain verve, but the most interesting antedate his entry into medicine. Of the current Russia which in the present status of world events one craves to know, nothing is said in this work. Dr de Savitsch is a White Russian, and he has been away too long. The reviewer confesses to no more than a mild interest in this book. A jaded appetite for this type of literature (unless something, really outstanding came along) may be responsible.

### NOTICES

#### SOUTH END MEDICAL CLUB

A regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 254 Columbus Avenue, Boston, on Tuesday, November 18, at 12 noon.

Dr H. Houston Merritt will speak on "Treatment of Epilepsy."

#### JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street Boston  
Lecture Hall, 9-10 a.m.

#### MEDICAL CONFERENCE PROGRAM, NOVEMBER

Wednesday, November 12—The Dynamics of Niral Respiration. Dr H. J. Sternstein.  
Friday, November 14—Some of the Disputed Points in the Treatment of Syphilis. Dr W. P. Boardman.

Saturday, November 15—Presentation and discussion of District and Boston Floating Hospital cases. Dr. P. Piccolo and Dr. Francis McDonald.

Wednesday, November 19—Refractory Blood Diseases. Dr. C. W. Heath.

Friday, November 21—Anemia and Hiatus Hernia. Dr. William P. Murphy.

Saturday, November 22—Blood Clinic. Dr. H. G. Brugsch.

Wednesday, November 26—What Happens to Alcoholics? Dr. Merrill Moore.

Friday, November 28—Gold Therapy of Rheumatoid Arthritis. Dr. Charles L. Short.

Saturday, November 29—Personal Experiences with Wartime Neuroses. Dr. Kurt Goldstein.

On Tuesday and Thursday mornings (except November 11 and November 20) from nine to ten o'clock, Dr. S. J. Thannhauser will give a medical clinic on hospital cases

### PETER BENT BRIGHAM HOSPITAL

Gordon Gordon-Taylor, O.B.E., M.A. (Abert.), M.S., B.Sc. (Lond.), F.R.C.S., F.R.A.C.S. (hon.), senior surgeon to the Middlesex Hospital, London, and surgeon rear-admiral to the Royal Navy, will be surgeon-in-chief *pro tempore*, at the Peter Bent Brigham Hospital, Boston, from November 9 through November 15. All physicians are cordially invited to attend the regular hospital exercises in which he will participate, that is, the clinicopathological conference on Monday, November 10, at 12:15 p.m., the surgicopathological conference on Wednesday, November 12, at 4:00 p.m., and the joint Peter Bent Brigham Hospital—Children's Hospital rounds (at the Children's Hospital) on Thursday, November 13, at 8:30 a.m.

### HARVARD MEDICAL SOCIETY

A meeting of the Harvard Medical Society will be held in the amphitheater of the Peter Bent Brigham Hospital on Wednesday, November 12, at 8:15 p.m.

#### PROGRAM

Clinical presentation.

Remarks Concerning Military and Naval Surgery. Mr. Gordon Gordon-Taylor, O.B.E., surgeon to Middlesex Hospital, London; surgeon rear-admiral to His Majesty's Navy; surgeon-in-chief *pro tempore*, Peter Bent Brigham Hospital.

Physicians and medical students are cordially invited to attend.

### BOSTON DOCTORS' SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse, under Alexander Thiede, every Thursday at 8:30 p.m. at Station WMEX, 70 Brookline Avenue, Boston. Those interested in becoming members should communicate with Dr. Julius Loman, 520 Beacon Street, Boston (KEN 3200 or L 2N 2155).

### MASSACHUSETTS DEPARTMENT OF CIVIL SERVICE AND REGISTRATION

Medical Inspector (Part-Time), Health Department, \$2000 a year, Boston

Director of State Civil Service, Ulysses J. Lupien, has announced that a competitive examination is to be held on December 13, to find eligibles for appointment to the position of part-time medical inspector, Health Department, Boston.

The entrance requirement is as follows: applicants must be registered physicians under the Massachusetts Board of Registration in Medicine. The subject and weights of the examination are as follows: training and experience, 2; practical questions, 3; total, 5. To become eligible, applicants must obtain a grade of at least 70 per cent in each subject. The last date for filing applications is Saturday, November 22, at 12 noon.

### NATIONAL COMMITTEE FOR MENTAL HYGIENE FELLOWSHIPS

A limited number of fellowships are being offered for training in extramural and child psychiatry. Initial selection for these fellowships is to be made by the National Committee for Mental Hygiene, and eligible applicants will be recommended for appointment in selected training clinics. These fellows will spend one or two years in a clinic, the term and plan of the fellowship to be determined by the peculiar needs of the applicant. The training is pursued according to a definite plan related to the probable future functions of these fellows. Candidates for fellowship award should have had at least a general internship and two years of psychiatry in an approved mental-hospital service, in addition to other qualities fitting them for extramural service. Since this provision of training fellowships comes in response to a definite paucity of personnel in this field, peculiarities of the demand are considered in making appointments. The stipends vary slightly with location and status of the fellow but in general range between \$2000 and \$2600.

Requests for further information about these fellowships, and applications therefor, should be addressed to Dr. Milton E. Kirkpatrick, National Committee for Mental Hygiene, 1790 Broadway, New York City.

### SOCIETY MEETINGS AND CONFERENCES

#### CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, NOVEMBER 9

##### MONDAY, NOVEMBER 10

12 15-1 15 p.m. Clinicopathological conference Peter Bent Brigham Hospital amphitheater

##### TUESDAY, NOVEMBER 11

12 15-1 15 p.m. Clinicorontgenological conference. Peter Bent Brigham Hospital amphitheater.

##### WEDNESDAY, NOVEMBER 12

\*9 00-10 00 a.m. The Dynamics of Nasal Respiration Dr. H. I. Sternstein. Joseph H. Pratt Diagnostic Hospital.

\*12 00 m. Clinicopathological conference. Children's Hospital

\*8 15 p.m. Harvard Medical Society. Amphitheater, Peter Bent Brigham Hospital.

##### THURSDAY, NOVEMBER 13

\*8 30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Children's Hospital. Conducted by Dr. Kenneth Blackfan

\*9 00-10 30 a.m. Medical clinic. Dr. S. J. Thannhauser Joseph H. Pratt Diagnostic Hospital

(Continued on page x)



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## A STUDY OF INFLUENZA IN BOSTON DURING THE WINTER OF 1940-1941<sup>1</sup>

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AND JOHN F. ENDERS, PH.D.<sup>4</sup>

BOSTON

**A**N epidemic of influenza during the fall and winter months of 1940 and 1941 affected almost every section of the United States. A sharp rise in the incidence of this disease was recorded in California during November, and a peak of about 37,000 cases was reported from the Pacific and Mountain regions for the week ending December 21. The regions of the Southeast presented a maximum of about 58,000 cases during the week of January 11, and the South Atlantic region one of about 50,000 cases in the week of January 25. According to the statement in *Public Health Reports*,<sup>1</sup> "In the East North Central, West North Central and New England regions the disease did not appear until about the middle of January and in the Middle Atlantic region the highest weekly incidence was reported during the week ended February 1st."

The total influenza morbidity reports as given by *Public Health Reports* for New England for the period from December, 1940, through March, 1941, are assembled in Table 1. These data suggest that the outbreak in New England became evident suddenly, rapidly attained a maximum about the middle of January, and subsided abruptly.

It will be noted that no figures for Massachusetts are included in the table, since in this state the disease is not reportable. Recorded deaths, however, from influenza in Boston were 4 in December, 22 in January, 11 in February

and 4 in March. The following statement, moreover, has been published: "It was reported January 11 that 18,000 school children in Boston were ill with a mild form of the disease. Classes had been suspended in Salem, Haverhill and Gardner, Massachusetts."<sup>2</sup> During January, the average

TABLE 1 Number of Cases of Influenza Reported in New England, December, 1940, through March, 1941

For Week Ending	MAINE	NEW HAMPSHIRE	VERMONT	CONNECTICUT	RHODE ISLAND	TOTAL
						WEEK MONTH
December 7	2	0	0	2	0	4
December 14	7	0	0	6	0	13
December 21	3	2	0	2	1	8
December 28	24	0	0	1	0	25
January 4	40	0	99	10	0	149
January 11	1345	1000	76	111	31	2563
January 18	1421	1000	81	1718	16	4236
January 25	1138	44	23	1869	29	3103
February 1	197	27	128	623	23	998
February 8	63	5	26	317	10	421
February 15	112	0	0	90	1	203
February 22	11	16	0	63	0	90
March 1	28	10	0	62	2	102
March 8	6	8	0	26	0	40
March 15	1	3	0	4	0	8
March 22	0	3	0	6	0	9
March 29	1	0	0	8	2	11

daily attendance of 134,000 grammar school and high school children in Boston decreased 8 per cent, as compared with the records for December and February.<sup>3</sup> Reportable communicable diseases were not unusually prevalent during this period.

During the outbreak in Boston, clinical and laboratory studies of respiratory illnesses occurring in two groups of adults, some of whom had been vaccinated against influenza, were carried out. In addition, serums from certain pneumonia patients entering a large city hospital throughout this period were examined serologically. The findings are described in this communication.

### METHODS

The two groups selected for study consisted of 404 students at the Harvard Medical School and 558 members of the personnel of the Boston City

<sup>1</sup>From the Department of Bacteriology and Immunology, Harvard Medical School and School of Public Health, the Department of Hygiene, Harvard University, the Thayer Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School.

<sup>2</sup>Formerly student, Harvard School of Public Health.  
<sup>3</sup>Instructor in medicine, assistant in preventive medicine and assistant medical adviser, Harvard Medical School.

<sup>4</sup>Instructor and Francis Well Peabody Fellow in Medicine and Instructor in Bacteriology, Harvard Medical School; assistant physician, Thayer Memorial Laboratory, Boston City Hospital.

<sup>5</sup>Assistant professor of Bacteriology, Department of Bacteriology, Harvard Medical School.

Hospital. Approximately half the former group received, on January 6, the "complex chick-embryo vaccine" (canine-distemper virus and influenza A virus).<sup>4</sup> About two fifths of the latter group were given this vaccine on January 8. Serums were taken immediately before the administration of vaccine, and four weeks later from the vaccinated and nonvaccinated medical students. Serums were

37°C. for one hour, 0.5 cc. of 2.5 per cent sheep cells sensitized with 2 units of amboceptor was added and incubation continued for forty-five minutes. Final readings were taken after overnight storage in the refrigerator. The test was considered significant when the titer of the second serum specimen was four or more times greater than that of the first serum taken. Complement-

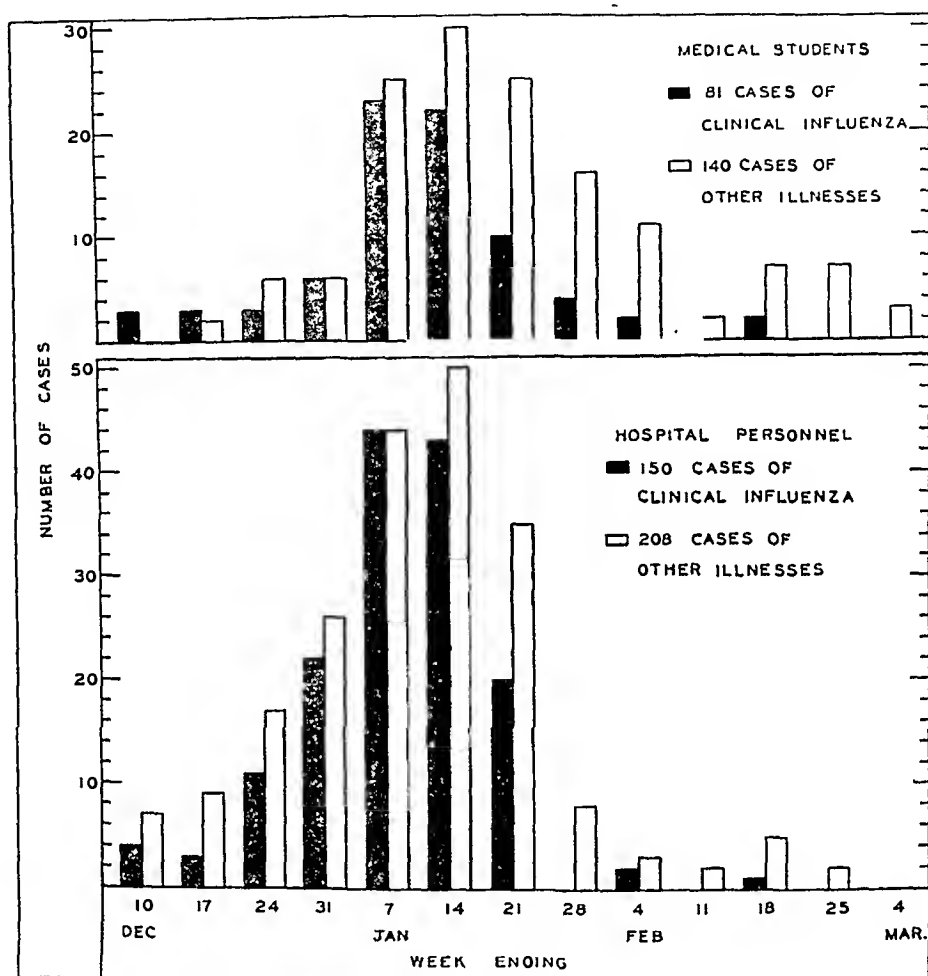


FIGURE 1. *Distribution of Cases of Clinical Influenza and Other Illness in Hospital and Student Groups according to Time of Onset.*

taken from the hospital group at the time of vaccination and again three weeks later. Complement-fixation tests with influenza A virus as antigen were carried out on all these serums, and, as previously mentioned, on certain serums from cases of pneumonia in the Boston City Hospital. The technic employed was similar to that of Eaton and Rickard.<sup>5</sup> To 0.25 cc. of serum was added 2 units of complement, saline to a total volume of 0.75 cc. and 0.25 cc. of antigen (a 2 per cent suspension of mouse lung infected with influenza A virus [Strain PR 8]\*). After incubation at

fixation tests<sup>6</sup> on some of the same serums, using influenza B virus (Lee strain),\* were carried out by the same procedure, except that a 5 per cent suspension of infected mouse lung was used as antigen. Serums known to be positive were included as controls in all tests, as well as normal mouse lung (2 or 5 per cent suspension) and the usual serologic controls.\*

The titer of a serum was recorded in terms of its final dilution in the volume of fluid present before the addition of the sensitized cells. The end point was taken as the dilution of serum that gave complete fixation in a final dilution of 1:16 and slight fixation in higher dilutions. Certain

\*We are indebted to Dr. Frank L. Horsfall, Jr., Rockefeller Foundation, New York City, for the influenza A virus and positive serums, and to Dr. Thomas Francis, Jr., New York University College of Medicine, New York City, for the influenza B virus.

investigators have expressed the titer in terms of the original dilution of the serum. Although we should like to adhere to this practice for the sake of conformity, it is evident that this makes it impossible to compare satisfactorily the results of different investigators unless comparable concentrations of reagents are universally employed.

Influenza A virus was isolated by the intranasal inoculation of ferrets with throat washings obtained from patients. With material from infected ferrets, mouse passages were initiated.

Virus neutralization tests in mice were done with serums of 2 cases from which virus was recovered; 0.05 cc. of a mixture of equal parts of infected mouse lung (1:1000) and dilutions of serum was inoculated intranasally. The neutralization titer of the serum was expressed in terms of its final dilution.

Cross-neutralization tests in mice were carried out with immune rabbit serums prepared by the single intraperitoneal inoculation of 10 to 12 cc. of a 10 per cent suspension of the lungs of mice infected with the several strains of virus examined. The rabbits were bled ten to seventy-two days following injection.

The persons studied were classified under three headings, according to the clinical history. Under "clinical influenza" were included all those who gave a history of illness characterized by sudden onset, fever above 99°F. and constitutional symptoms such as weakness, and muscle, bone or joint pains. Under "other illness" were assigned those who had any illness of the respiratory tract other than clinical influenza, as characterized by all the foregoing criteria, or of an ill-defined nature. Under "no illness" were listed those who had no illness during the period of observation.

In both the student and hospital groups, serologic data secured for the month of January are presented. The students returned to school on January 3, after the Christmas recess. A few had been ill either in Boston or elsewhere during the recess, and were accordingly excluded from the serologic study.

## RESULTS

Figure 1 presents by weeks the number of cases of clinical influenza and other illness in the hospital and student groups for the period of three months, according to the time of onset. The distribution of cases according to the clinical classification is similar. In the hospital group, 90 per cent of the cases of clinical influenza and 80 per cent of the cases of other illness occurred from December 17 to February 1. For the student group,

the figures are 79 and 66 per cent, respectively. The peak of maximum illness in both classes occurred about the middle of January. There is thus a suggestive chronologic parallelism between the incidence of influenza and other respiratory illness.

The incidence of illness during January is presented in Table 2. It is evident that about half the patients in each group were ill, and that in about one sixth of both groups these illnesses were diagnosed as influenza.

The results of complement-fixation tests for influenza A virus with serums from the student and

TABLE 2. Incidence of Illness in Medical Students and Hospital Personnel during January, 1941.

ILLNESS	MEDICAL STUDENTS		HOSPITAL PERSONNEL	
	NO. OF CASES	PER CENT	NO. OF CASES	PER CENT
Clinical influenza	58	14	108	19
Other illness	125	31	137	25
No illness	221	55	313	56
Totals	404		558	

hospital groups are given in Table 3. On the assumption that a fourfold rise or more in titer of complement-fixing antibodies indicates recent influenza infection,<sup>2</sup> 18 per cent of the nonvaccinated group had had recent contact with this

TABLE 3. Results of Complement-Fixation Tests for Influenza A Virus.

GROUP AND DIAGNOSIS	NO. RISE IN TITER		FOURFOLD OR GREATER RISE IN TITER		TOTALS
	NO. OF CASES	PER CENT	NO. OF CASES	PER CENT	
Medical students					
Vaccinated group	90	53	81	47	171
Clinical influenza	2	1	19	11	21
Other illness	27	16	34	20	61
No illness	61	36	28	16	89
Nonvaccinated group	128	81	30	18	158
Clinical influenza	7	4	13	8	20
Other illness	36	23	10	6	46
No illness	85	54	7	4	92
Hospital personnel					
Vaccinated group	11	25	33	75	44
Clinical influenza	2	5	13	29	15
Other illness	1	2	2	5	3
No illness	8	18	18	41	26

strain of virus. Thirty-five (22 per cent) of the 158 in this group showed titers of 1:64 or higher. Seven nonvaccinated and 4 vaccinated persons having clinical influenza experienced no rise in titer. Three of the former had initial titers of 1:64.

In none of these 11 cases was a rise in complement-fixation titer for influenza B virus demonstrated, yet clinically the illnesses could not be distinguished from those in cases that revealed

a significant rise in titer for influenza A virus. Moreover, all the serums from the 44 persons in the vaccinated group at the hospital, together with those from 82 pneumonia patients in the same institution, were tested for complement fixation with influenza B virus. None exhibited a rise in titer, although 4 had titers (1:64) above 1:16. These findings suggest that influenza B virus in all probability played no etiologic role in the groups studied.

About one fifth (10) of the 46 nonvaccinated persons having other illnesses showed significant rises in titer. All but 3 of these, however, had symptoms of clinical influenza, but no temperatures were recorded. It is noteworthy that about 8 per cent (7) of the 92 nonvaccinated persons with no history of illness also had serologic evidence of a reaction to influenza A virus.<sup>5</sup>

Vaccination alone seems to increase complement-fixation titers in certain persons, as shown by comparisons between the vaccinated and nonvaccinated groups as a whole and between the various clinical classifications (Table 3). For example, 47 per cent of the vaccinated group of medical students exhibited a fourfold rise or more in titer compared with 18 per cent in the control group. In the vaccinated group of students who had no illness, 16 per cent showed rises, whereas in only 4 per cent of the corresponding class in the nonvaccinated group did similar changes occur. The high incidence of increases in titer found for the class with no illness at the hospital, as contrasted with that for the corresponding class in the medical-student group, may possibly be accounted for by the probable greater chance of exposure in the institution, which would tend to a larger number of inapparent infections.

#### CLINICAL ASPECTS

A review of 50 case histories of the students with clinical influenza revealed that all but 2 had a sudden onset, and a fever (100 to 102°F.) lasting three days was common. A few had temperatures as high as 104°F. The duration of fever did not exceed four days. Headache, muscle or joint pains and sore throat were characteristic complaints. The acute symptoms usually subsided with the fever, or one to two days later. The majority developed coryza and a cough that usually was not productive and persisted one to two weeks. Weakness was a major complaint and lasted more than one week in about half the cases. Thirteen students were hospitalized. Complications occurred in only 1 patient, who developed otitis media and recovered.

The duration of illness, as indicated by absence

from duty in 117 cases of clinical influenza in the hospital group, is shown in Table 4. In 40 per cent, disability lasted over one week, and in 9 per cent over two weeks.

Of 358 persons in the hospital group with clinical influenza (150 cases) or other illnesses (208

TABLE 4. *Duration of Illness with Clinical Influenza in Hospital Group, December, 1940, through February, 1941.*

DAYS ABSENT FROM DUTY ON ACCOUNT OF ILLNESS	No. OF CASES	PER CENT*
0-4 .....	21	18
4-8 .....	53	45
8-11 .....	24	20
11-15 .....	10	9
15-22 .....	7	6
More than 21 .....	2	2
Total .....	117	

\*Absent from duty less than 8 days, 63 per cent; absent from duty less than 15 days, 92 per cent.

cases) during December through February, 7 cases of pneumonia and no deaths occurred. Three of these complicated influenza, of which one was severe. One other patient had a Type 8 pneumococcus in the sputum. Bacteriologic examination of the sputums of the other patients did not reveal any organisms responsible for the pneumonia. Unfortunately, no serums from these patients were available for study.

Serums from a number of patients with pneumococcal pneumonia admitted to the Boston City Hospital from December through April were available for study. These serums had been collected at random, primarily for studies in pneumococcal immunity by Dr. Maxwell Finland and his associates. From each patient, however, a typable pneumococcus was obtained by culture of the sputum, throat swab or blood. In addition to the various types of pneumococci (Types 1, 2, 3, 4, 5, 7, 8, 14, 18 and 19), cultures of the sputum or throat yielded in some cases alpha-hemolytic streptococci, *Haemophilus catarrhalis*, *H. influenzae*, staphylococci or diphtheroids—the usual flora of the respiratory tract.

During the same period, an unusually large number of cases of staphylococcal pneumonia occurred, often associated with clinical influenza or occurring as a complication thereof. Cultures of the sputum or blood from these patients yielded hemolytic *Staphylococcus aureus* as the predominant organism, although in a few patients alpha-hemolytic or beta-hemolytic streptococci or *H. influenzae* was also present in the respiratory tract. Details of the clinical features of these patients have been reported by Finland, Strauss and Peterson.<sup>7</sup>

Serums from a few of the cases of staphylococcal

pneumonia, together with all those from the cases of pneumococcal pneumonia, were tested for complement fixation with influenza A virus. In certain cases, there was only a single specimen, and in others several specimens obtained over a period of more than a month were examined.

The results are given in Tables 5 and 6. The high incidence of complement-fixation titers of

influenza A virus. The first specimen of these pairs of serums was obtained less than ten days, and the second more than fourteen days, after the onset of illness. One of these cases occurred in April, well after the influenza outbreak had subsided. Of the 9 patients with staphylococcal pneumonia, 3 showed rises and 3 showed decreases in titer that were considered significant.

TABLE 5. Results of Complement-Fixation Tests for Influenza A Virus with Serums of a Group of Pneumonia Patients Admitted to the Boston City Hospital from December, 1940, through April, 1941.

MONTH	TYPE OF PNEUMONIA*	HIGHEST COMPLEMENT-FIXATION TITER FOUND IN SERUM							TOTAL NO. TESTED	TITER <1:64	TITER OF 1:64 OR HIGHER	TITER OF 1:64 OR HIGHER PER CENT
		<1:16	1:16	1:64	1:128	1:256	1:512	1:1024				
December	S	1	0	0	0	1	0	0	2	1	1	50
	P	5	3	0	0	1	1	0	10	8	2	20
January	S	0	1	0	3	1	2	0	7	1	6	86
	P	2	3	2	2	3	3	1	16	5	11	69
February	P	2	7	3	2	0	1	0	15	9	6	40
March	P	5	10	8	2	0	0	0	25	15	10	40
April	P	3	8	4	1	0	0	0	16	11	5	31
Totals	S	1	1	0	3	2	2	0	9	2	7	78
	P	17	31	17	7	4	5	1	82	48	34	42
	All	18	32	17	10	6	7	1	91	50	41	45

\*S = staphylococcal pneumonia, P = pneumococcal pneumonia

1:64 or more (34 of 82 patients, or 42 per cent) is suggestive of a recent reaction to this virus. This high incidence is particularly evident in the staphylococcal group (7 of 9 patients, or 78 per cent); one patient, whose serum had a titer of

TABLE 6. Results of Complement-Fixation Tests with Serums of Selected Pneumonia Patients.\*

DATE	CASES WITH NO CHANGE IN TITER	CASES WITH FOLDFOLD OR GREATER RISE IN TITER	CASES WITH HIGH INITIAL TITER AND LATER SIGNIFICANT DECREASE	TOTAL CASES
December	4	1	0	5
January	0	3†	3†	6
February	1	2	0	3
March	6	1	0	7
April	5	1	0	6
Totals	16	8	3	27

\*Two samples tested, of which the first was taken ten days or less and the second fourteen days or more after the onset of illness.

†Cases of staphylococcal pneumonia.

1:16, died, and the presence of influenza A virus was presumptively demonstrated in the lungs.\*

Eight of 24 serums from the pneumonia cases for which two samples were available showed a significant rise in complement-fixation titer for

\*A ferret inoculated intranasally with a suspension of the lung of this patient developed no signs of infection, but proved refractory to subsequent inoculations with influenza A virus (Strain PR 8). The ferret's serum taken prior to the second inoculation protected mice against infection with this strain of virus.

As previously stated, complement-fixation tests with influenza B virus were done on all serums from the pneumonia patients. No rises in titer and no high titers—3 had titers of 1:64—were found. Furthermore, no correlation could be established between the type of throat flora and the presence of either a high antibody titer or an increase in titer for influenza A virus in the blood of these patients.

#### STUDIES WITH VIRUSES ISOLATED FROM THROAT WASHINGS

Two strains of influenza virus were isolated from the throat washings of 2 patients seen on January 3 and January 11, respectively. Ferrets that were inoculated intranasally responded in the first passage with fever and signs of nasal involvement. Ferrets were inoculated in series at intervals of two to five days, turbinates or a mixture of turbinates and lung tissue being used for transfer. All exhibited signs of infection. If only a small quantity of virus was present, however, in the throat washing (for example, after passage through a Berkefeld filter), no sign of infection in the first passage was seen, but when the ferret was allowed to recover, its serum contained neutralizing antibodies, as demonstrated by the mouse-protection test.

The convalescent serums of ferrets recovered from infection with either strain of virus had

high titers of neutralizing antibodies when tested against influenza A virus (Strain PR 8) in mice. In addition, both persons from whom virus was obtained had a significant rise (1:4 to 1:64 and 1:16 to 1:64, respectively) in titer of neutralizing antibodies, as well as a rise in complement-fixation titers when tested with this strain of virus.

Passage of virus from ferrets to mice did not succeed until the fifth and sixth ferret passages. Mice did not die until three mouse passages had been carried out. The virulence of the virus in infected mouse lungs gradually increased. Thus, 0.05 cc. of infected mouse lung of the twelfth passage, diluted 1:1000, was lethal for mice, whereas the same volume of lung suspension from the twentieth passage killed in a dilution of 1:100,000.

The antigenic relations of the two strains of recovered virus and of the influenza A virus (Strain PR 8) were investigated by means of cross-neutralization reactions, with immune rabbit serums prepared against each strain. The results of these tests are not presented in detail. They indicated, however, that antigenic differences existed among the three strains.

#### DISCUSSION

The epidemiologic, clinical and laboratory findings presented in this paper show that an outbreak of acute upper respiratory disease, studied in Boston during the winter of 1940-1941, was in part due to epidemic influenza. In the majority of cases diagnosed as influenza, influenza A virus appeared to be the etiologic agent. This is based on the following facts: viruses of this type were isolated from the throat washings of 2 typical cases; many patients exhibited rises in complement-fixation antibodies for the influenza A virus following their illnesses; and in a fairly large number of serums, no complement-fixing antibodies could be demonstrated for influenza B virus.

In accordance with the epidemiologic pattern noted in previous outbreaks, the characteristic rapid rise and fall in incidence was observed. Relatively few cases were noted during the last two weeks in December. Increasing sharply to a maximum in the second week of January, the number of cases had by the end of that month again reached a low level of incidence. It is of interest in respect to the problem of the interepidemic persistence of this disease that scattered cases occurred as late as April 1. During the month of January, about half the persons under observation had either influenza or some other illness. Many of these infections, however, were apparently not due to known strains of the influenza virus. This parallelism between influ-

enza and other illnesses may, of course, be attributable to chance, but since similar phenomena have been described by others, it is possible that the same factors responsible for the spread of influenza were operative in that of the undefined infections.

From a clinical standpoint, the uncomplicated disease was in general mild, but otherwise typical of influenza as described in other recent outbreaks.<sup>8-10</sup> In the combined hospital and student groups, only 7 cases of pneumonia occurred during the observation period of three months. Of these, only 3 appeared to complicate clinical influenza.

Examination of serums from 82 patients with pneumococcal and 9 patients with staphylococcal pneumonia revealed that an unusually large number had titers high enough to suggest recent exposure to the influenza A virus. In 27 of these patients, samples of serums were available and were adequate for testing whether or not a close association between the virus and the bacteria was present at about the same time. In 5 of 21 cases of pneumococcal pneumonia, the serologic evidence indicated an associated infection with influenza A virus, and such evidence was obtained in all 6 patients with staphylococcal pneumonia. Although a causal relation between the influenza and the pneumonia has thus not been demonstrated by either clinical or laboratory evidence, it seems possible that in certain of these patients, at least, influenza represented a factor predisposing to the pneumonia.

One of the important objectives, of course, in studies of this kind is to accumulate information that may lead ultimately to means of more certain recognition of the disease. It is therefore pertinent to compare the results obtained in this investigation by means of complement-fixation tests with the clinical diagnosis.

The cases studied during the epidemic period were classified clinically as clinical influenza and other illness. In the unvaccinated student group, it was found that 7 among 20 of those comprising the former class exhibited no increase in complement-fixation titer, whereas 10 among 46 of the latter class showed a significant rise. These findings, then, do not seem to indicate a close correlation between the two methods of diagnosis.

This discrepancy may be attributed to several factors. One of these is the inadequacy of certain of the clinical records. For example, 7 of the patients with other illness who showed rises in titer had all the clinical manifestations regarded as diagnostic of influenza, but their temperatures were not recorded. Had the records been avail-

able, these patients would without much doubt have been included in the influenza group, and thus the percentage of correlation would have been raised from 65 to 74. Then only 3 who showed an increase in titer would have been left in the group of 39 patients with other illnesses, giving a correlation of about 92 per cent between the serologic and clinical diagnoses.

Imperfect recording, however, cannot offer an explanation for the fact that 7 patients in the clinical influenza class apparently underwent a disease typical in all respects of influenza, yet showed no evidence of antibody increase for either influenza A or B virus. This behavior may be accounted for by failure of these persons to produce antibodies detectable by the methods employed, or it may be the result of infection with one or more serologically distinct types of virus, as yet unidentified.

However this may be, at the moment the correlation between the serologic diagnostic test and clinical diagnosis, not only in this study but also in that carried out recently by Dalldorf and his associates,<sup>10</sup> is not so close as one might wish.

The fact that in the nonvaccinated student groups 8 per cent of those having no illness gave serologic evidence of recent contact with influenza A virus is in accord with the figure of 6 per cent in analogous groups recorded by Eaton and Rickard.<sup>5</sup> The epidemiologic role of this sort of patient requires investigation, since he might represent an important factor in the transmission of the virus were his function as a carrier demonstrated.

It should be noted that in this discussion we have confined ourselves to the data obtained in the nonvaccinated group. This was necessary because our findings suggest that vaccination might lead to a fourfold or greater increase in titer of complement-fixing antibodies, thus rendering doubtful the significance of the data obtained in the vaccinated group in respect to the association between rises in titer and clinical diagnosis.

The increase in complement-fixing antibody in certain persons following vaccination is in contrast to the findings of Morrison and his co-workers<sup>11</sup> that repeated vaccination with active chick-embryo virus (influenza A virus [Strain PR 8]) did not induce the formation of this antibody, although neutralizing substances made their appearance.

Our experience with vaccination once again illustrates the futility of attempting to induce active immunity in the face of an outbreak of a disease characterized in its epidemic pattern by sudden appearance and rapid defervescence. Since antibodies do not normally appear before about the

seventh day following the onset of illness, vaccination probably would not lead to an effective state of resistance before this time. Indeed, even a longer interval is perhaps required. All but 8 cases of influenza occurred among the vaccinated persons during the two weeks following vaccination. The data therefore do not present a basis for an adequate estimate of the value of the mode of vaccination employed, but it is noteworthy that clinical influenza may occur in persons who have been vaccinated two weeks before the beginning of their disease. In evaluating this fact, however, one must remember that, because of the rise of antibody induced by the vaccine, we could not determine by serologic test whether the etiologic agent in these cases was influenza A virus. Nevertheless, because of the high incidence of nonvaccinated cases due to this agent, the probability is that certain of these patients were infected with influenza A virus.

Dalldorf and his associates<sup>10</sup> have recently analyzed the incidence of influenza A among persons who had received the complex vaccine of Horsfall and Lennette several weeks before their illness. Protection was not evident as a result of vaccination, but the authors believed that complications were prevented.

Although there can be no doubt that the two strains of virus isolated from patients during the epidemic belonged to the group of viruses now designated influenza A, they exhibited differences indicating that they were not identical. Cross-neutralization tests with antisera prepared in rabbits against these and Strain PR 8 suggested definite though minor antigenic differences. Magill and Francis<sup>12</sup> have described analogous dissimilarities in antigenic composition in various strains of influenza A, and even in those derived from cases in the same epidemic. Our observations, then, add to the evidence for the marked heterogeneity of strains of influenza A, which possibly depends either on the existence of very large numbers of different strains with fixed antigenic properties or on an extreme tendency to variation on the part of a single virus.

#### SUMMARY

An epidemic of influenza occurred in Boston during December, January and February, 1940-1941, which appeared to be a part of an outbreak extending throughout most of the United States.

In Boston, three groups were studied: medical students, hospital personnel and patients hospitalized for pneumonia.

The uncomplicated disease was mild. Complications were rare among the medical students and

hospital personnel, but in a series of 91 pneumonia patients, serologic evidence indicating that a large number had had contact with influenza A virus suggested a possible relation between the two diseases.

Influenza A virus was isolated from 2 patients and was shown by serologic tests to be the chief etiologic agent in the outbreak.

No evidence for infection with influenza B virus was obtained, although certain patients with typical manifestations of clinical influenza gave no indication of a recent infection with influenza A virus.

The correlation between the clinical and serologic means of diagnosis was incomplete.

Eight per cent of nonvaccinated medical students who had no illness of any sort during the period of observation presented serologic evidence of recent contact with influenza A virus.

Vaccination with the complex vaccine of Horsfall, Lennette and Rickard appeared to induce the formation of complement-fixing antibodies in a certain proportion of persons.

The prophylactic value of this vaccine cannot be

determined from the data presented, since vaccination was undertaken at the inception of the epidemic. Eight persons, however, developed clinical influenza two weeks or more following vaccination.

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## SYMPOSIUM: THE CONDITIONED REFLEX OF PAVLOV

### THE PHYSIOLOGIST'S POINT OF VIEW\*

ROY G. HOSKINS, M.D.†

BOSTON

IT is rather a large undertaking to present the fundamentals of the conditioned reflex or its more complex manifestation, conditioned behavior, in a few minutes. The doctrine of conditioned behavior is a relatively simple one, made up of only a few components but conventionally couched in a rather unattractive terminology. Conditioning can lead to such unexpected, bizarre and apparently illogical results that the hard-headed realist has some difficulty in admitting to himself that it represents sound biology.

To put the matter in everyday terms, I might stand at the ceiling and say, "Ugh." I should expect that procedure a primary unconditioned response of surprise,—but that I changed the syllable slightly to expect the reaction to be quite different. The syllable brings up a men-

tal image of the quadruped with fur who barks and becomes odoriferous when he is wet. To that second syllable, most human beings have been conditioned in a variety of ways, the end reaction being mostly mental imagery.

As another example of conditioning, I might guarantee, with two ounces of cellulose and a few grains of coal-tar derivatives, to produce in a man an increased pulse rate, deepening of the respiration and dilatation of the pupils—without having the materials within a hundred feet of the subject. The special circumstances would be that the subject, a lonesome American, traveling abroad, should suddenly come on "Old Glory" floating in the breeze. The conditioning, in this case, would have been due to the various experiences by which the citizen had learned the meaning of the American flag. "Learning" and "conditioning" are but two words for the same process. The learning, however, may include much more than the acquiring of conventional lore. It may

\* Papers were presented at the Section of Society, Boston, May 21, 1941.

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involve and be expressed by any active process in the body. In the flag example, the response involves smooth, cardiac and skeletal muscles.

The subject of conditioning is conventionally presented in terms that do not seem to mean a great deal. The classic example is ringing a bell and making a dog salivate—a happening seemingly remote from the field of practical pediatrics. However, for delineating the problem, I believe that the Pavlov dog can be profitably brought to the scene again. In Pavlov's earlier studies on the physiology of the digestive system, his experiments had been interfered with a great many times by the so-called "emotional reactions" of his dogs. About 1904, he decided to make a study of these confusing matters, and out of this study grew many years of work on conditioned behavior. One of his earlier procedures was to put some acid on the tongue of a dog and measure the resulting salivary secretion. Then, at the same time that the acid was given, a bell was rung, the procedure being repeated many times. After a while, the ringing of the bell alone caused increased salivation.

But essentially the same phenomenon is a matter of common experience. Ordinarily, when a man in his study hears the dishes in the kitchen begin to rattle, he is merely annoyed at the distraction. Suppose, however, he has been out skiing and is resting by the fire when he hears the noise from the kitchen; he suddenly realizes that his salivary glands are secreting, as are his gastric glands. So much, then, for conditioning of glandular functions.

Again, a man may be strolling down the street in the evening when a whiff of lilac perfume is wafted on the breeze. His higher brain may have lost all recollection of the pleasant evening in the moonlight years before by which the conditioning was established, but somewhere in the brain the trace has persisted and he reacts with a thrill of pleasure—in this case, perhaps a purely affective response, although with secondary somatic reverberations. Still enjoying the thrill, the man enters his home and sees the new maid looking sweet and attractive and has a little episode with her. The next morning, when the maid serves the breakfast, he gets red in the face. The conditioning this time expresses itself objectively via the vasomotor system.

A classic example of conditioning of still another sort is that of the boy who was given castor oil in canned peach juice. For fifteen years, he

could not taste peaches without nausea. But more than that, he also "tasted" castor oil each time. Here the conditioning was perceptual—a falsification of sense impression.

Another often cited case is that of Watson's baby, "Albert."\* The baby had had the benefit of a faultless environment up to the time he fell into the hands of the psychologist and had only two fears in the world—fear of loud noises and of falling—with which all babies are born. Watson put the baby on a table and then placed a rabbit beside him. Just as the baby reached for the rabbit, a steel bar was sharply struck behind his head. He started and drew back. The rabbit was brought up again, and just as the baby reached for it, the noise was repeated. This time, the baby drew back and fell on his side. The experiment was renewed (What the mother was doing in the meantime is not stated). Finally, every time a rabbit was brought near him, he went into a marked fear reaction: he cried, fell over and could not be induced with any sort of encouragement to touch a rabbit. Not only was he conditioned against rabbits, but his fear was generalized to include any kind of furry object—white rats, kittens, Santa Claus whiskers and so forth.

Such conditioned fears are of widespread occurrence and are of great clinical significance. Very often, the episode that caused the fear is not remembered, and the end result is called a phobia. Such phobias are seemingly utterly illogical, but they are very real and may go far to wreck the life of the patient.

In all the foregoing examples, the conditioning has been accompanied by awareness on the part of the subject. Such awareness, however, is not a necessary feature. By the simultaneous use of a sound signal and a flashlight, the pupils of a man can be conditioned to contract to an auditory stimulus, even when the subject is totally unaware of the purpose of the experiment and despite the fact that one has no voluntary control of the pupils. Unwitting conditioning of involuntary activities is probably a rather common happening.

So much for conditioning of positive responses. It is possible, and the possibility is clinically meaningful, also to set up conditioned inhibitions. For example, a dog may be conditioned to salivate when a point, X, on his skin is touched. He is then trained to discriminate between spot X and another spot, Y. Y becomes a so-called "negative spot." If Y is first stimulated and then X, no saliv-

\*This case is cited from *The Psychology of Adjustment* (Schafer, L. H. *The Psychology of Adjustment* 600 pp. Boston: Houghton Mifflin Company, 1936).

hospital personnel, but in a series of 91 pneumonia patients, serologic evidence indicating that a large number had had contact with influenza A virus suggested a possible relation between the two diseases.

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tal image of the quadruped with fur who barks and becomes odoriferous when he is wet. To that second syllable, most human beings have been conditioned in a variety of ways, the end reaction being mostly mental imagery.

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ideal, and one is thus not surprised that these patients became conditioned to emotional settings, the one of fear and the other of rage.

May not the so-called "nervous element" in asthma be in large part conditioning—that is, a conditioned reflex? Examples of both certain and probable conditioned reflexes in the field of allergy are numerous and, to the initiated, easy of detection. One of our patients had asthma repeatedly in her own home,—in emotional environment,—whereas in a foster home a few miles away she never had an attack. Another girl had hives while at boarding school, but when she went home, they disappeared, they returned as soon as she boarded the train to go back to school. The cause of the original urticaria is not clear, but it was probably coincident with an emotion, possibly of homesickness, hence the conditioning. One may ask, "Assuming that you are right, and that this is a conditioned reflex of the skin capillaries, how shall we treat her?" The basic treatment should be not so much by calamine lotion, calicum or uncture of belladonna, but by avoiding the emotional reaction if it can be found. The woman sensitive to onions might respond merely from insight into the reflex, the girl with asthma accompanying fear, by obtaining reassurance, and the girl with asthma caused by rage, by intelligently thwarting the tantrums.

But one finds conditioned reflexes of the respiratory tract, when an element other than allergy is primary. The following case is duplicated in the practice of nearly every physician. The patient had an attack of influenza, early in January. Sinusitis and adenitis followed. Hemolytic streptococci were found. Fever lasted two or three weeks. Then the temperature became normal, and in February the child was sent back to school. She returned home with a "cold" that evening, then fever returned. Again, when she was better, she went to school. And again she got a "cold" and had another bout of fever. Once more, on returning to school, she was sick after only one day. The parents were distraught. Should she again return to school?

Does the child suffering from recurrent "colds" get a fresh virus infection each time she returns to school? Is she sensitive to school dust, sustaining each time a reflex irritation from such dust? Or, may she have a conditioned reflex to the school environment, where the first attack became manifest? The fever is a bit easier to explain, it was doubtless from the secondary invaders (bacteria of which the patient is a carrier), which became active as soon as the mucous membrane became reflexly engorged. The onset of each

recurrence was apparently conditioned, the course was guided by the secondary bacteria. A prolonged summer vacation, with changed environment, sunshine and warm weather, resulted in good health, and the patient became unconditioned. The next year's school session was passed without any infection, perhaps prophylaxis by a cold vaccine was given credit for the cure.

Another example is an adult patient who had continual recurrent infections one winter, the first attack was a virus infection, the others were characterized by swelling of the mucous membranes of the nose and throat (sinusitis?). Each attack followed a shopping trip to Boston.

Everyone is familiar with the people who get colds whenever they sit in a draft. The draft reflexly leads to mucous-membrane congestion. The proverbial contest between the persons who want the window open and those who want it closed shows that everybody does not experience this reflex. It is hard to believe that a virus comes in the window and picks out only certain people. Have these persons a conditioned reflex to the cold air, and does it refer back to the chill of an original influenzal infection?

A physician recently told me that he developed a pain in the muscles on the right side of the neck on exposure to a draft. It was definitely outlined as the sternocleidomastoid muscle. The pain was a soreness, as if the muscle were fatigued from overuse. There had apparently been a tonic spasm of the muscle, reflexly caused by the cold air. Was this a conditioned reflex? Did the conditioning date back to a spasm (torticollis) from a mild adenitis under that muscle?

Attacks of angioneurotic edema are very likely to be manifestations of a conditioned reflex. A leading scientist told me that he developed puffiness of the eyes and fullness of the throat when facing the stress of an important lecture.

About seven years ago, I read a paper before a Maine medical society on diarrhea in infants and children. I covered the causes of death—dehydration, toxemia, acidosis and inanition—and the treatment. At the end of the talk, one of the local physicians got up and said "You have told us nothing about nervous diarrhea. Why is it that when I get excited I have diarrhea?" In reply, I intimated that this was not common in children. However, I have thought it over a great deal since then. I now believe that nervous diarrhea is quite frequent in children.

We have all seen infants with summer diarrhea, those of us in pediatrics before 1920 have seen many. The baby gets diarrhea, it is starved, the diarrhea is checked. Then feeding is cau-

tiously resumed. Diarrhea tends to return, and nutrition is not maintained, although dehydration and toxicity are no longer present. If one observes these cases carefully, one may note movement of the bowels whenever the baby is fed, or whenever it is handled. Is this nervous diarrhea, peristalsis due to a conditioned reflex of the bowel muscles? Too often, the diarrhea returned when the patient was considered cured. Was this re-infection? Or may it have been conditioning? I recall one group of infants with summer diarrhea who persisted in having loose stools and malnutrition until January. Then all contracted measles, and were cured. Change of habits incident to the latter disease apparently unconditioned them.

If one has traveled a great deal in Europe, he will have consumed much sour cream and sour-cream ice cream. Two such travelers developed dysentery lasting three to five days. But every time ice cream was eaten over the next several years, a diarrheal movement shortly followed, with much of the pain and distress of the original dysentery but with no fever. One may therefore well ask, How many of our so-called "sensitivity-to-food episodes" may be conditioning rather than real allergic or toxic actions?

I recently had under my care a newborn baby. It was breast fed and had regained its birth weight at nine days of age. Then it developed loose stools—seven or eight a day—and stopped gaining. It had a stool every time it nursed. It appeared conditioned to have a stool every time it was fed; the nutrition was affected. To maintain nutrition, it was necessary to inhibit the reflex. Change of feeding habits or timing, bottle feedings, barium and bismuth were all considered. In this case, lime water gave relief.

In my own experience, a tendency for loose stools has on occasions been quite suddenly checked by a relatively heavy meal. A change of eating habits, type of food or time of eating seems occasionally to inhibit the hyperperistalsis. Does the banana or raw-apple feeding of diarrheal infants act to inhibit conditioned diarrhea?

Conditioning is apparent not only in diarrhea but also in habitual vomiting. One of my infant patients had been doing nicely until one day he vomited his orange juice; the next day, he also vomited his orange juice; other food had not been vomited. I recommended a change from orange juice to tomato juice, and the vomiting ceased.

The following story will be appreciated by those who have had to undergo intensive treatment with some of the new "magic" drugs. A ten-year-old patient had arthritis and tonsillitis. He was soon

receiving by physician's orders eight aspirin tablets, twelve sulfanilamide tablets, six yeast pills, four of vitamin B<sub>1</sub>, four of vitamin B<sub>2</sub>, four of nicotinic acid, eight of ascorbic acid and enough others to total fifty pellets a day. Each time, the pills went down harder and harder. By and by, it took half a glassful of water to down each pill. Gagging and occasional vomiting occurred. Anorexia followed. The sight of a pill was the sign for gagging, and conditioned vomiting was being established; when all pills were omitted, normalcy was restored.

The training of the infant in bowel habits is an application of the conditioned reflex. The youngster is placed on a chair, or pot, and a soap stick is inserted rectally. The irritation of the soap stick sets up rectal peristalsis, and the bowels move. The next day, the same procedure is carried out. The following day, just putting the child in his chair is sufficient to lead to rectal peristalsis, and the conditioning is accomplished.

The conditioning of the older child and the adult to regular bowel movements is much the same. But this conditioning can easily be broken if the patient makes a visit,—it is usually the "change of water," if one can believe what one is told,—if he oversleeps, as on a Sunday, if he is forced to share the bathroom facilities with visitors, or if he neglects the call of Nature.

It is now realized that the epileptic has some lesion in the brain or meninges that is the basis of the convulsive seizures. The actual attack is brought on by a reflex action originating elsewhere; these precipitating causes are numerous and include fatigue (eyestrain, poor posture), foci of infection, emotional reactions and constipation.

A few years ago, Dr. Frank Fremont-Smith<sup>2</sup> reported to the New England Pediatric Society the case of a young lady who had epileptic attacks on two different mornings after going on "blind dates." It was learned that she previously had become very much in love with a young man, and had been upset when he gave her up; she had met him while on a blind date. She died of a brain tumor six months later. The cause of the epilepsy was the brain tumor, but the convulsive attack was precipitated by the blind date. Another epileptic girl had an attack whenever she heard a loud or unusual noise, such as that caused by a falling kettle cover, by a boy falling from his bicycle or by a door slamming. The most frequently mentioned precipitating cause of an epileptic attack, however, is constipation. Is it due to autointoxication or conditioning?

In handling epileptic patients, one should con-

sider a conditioned reflex not as the cause of the brain lesion but as a possible factor in precipitating the attack.

Dentists see numerous cases of conditioning, resulting in syncope and diarrhea. Apprehension is undoubtedly the cause of the conditioning.

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With a recurrent complaint, such as upper respiratory infection, vomiting, diarrhea, allergic manifestation or convulsion, one should consider the possibility that a conditioned reflex has been established. A conditioned reflex may also be the basis of the onset of a bacterial infection. The so-called "nervous diseases" are frequently manifestations of conditioned reflexes.

One may rest assured, however, that not all conditioned reflexes are bad, any more than all habits are bad. Many conditioned reflexes are quite useful adjuncts to a normal and happy existence.

It is not particularly difficult to recognize that a patient's trouble is due to a conditioned reflex; it is often quite difficult to identify the causative stimulus, and even more difficult to remedy or inhibit the reflex.

One cannot help wondering if much of the relief from faith healing and from physiotherapeutic treatments is the result of inhibiting a conditioned reflex.

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## CONDITIONED BEHAVIOR\*

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NOTHING intrigues the clinician more than a clinical case, and since I am today addressing men whose interests are primarily clinical, I shall outline as briefly as I can—and I hope more briefly than one would expect of a child psychiatrist—a case from which may come a realization of the importance of early life conditionings in the later personality deviations of childhood. It should be remembered that psychiatrists deal with complex pattern reactions rather than with the simple conditioned responses referable to one sign or symptom, and that I cannot give all the material—many times but slowly and painfully produced by the patient—that brings the conditioning factors into relief.

Frank, a 15-year-old boy, was referred to the Judge Baker Guidance Center by a welfare agency that asked for advice about disposition of the boy because he was a serious behavior problem at a trade school. According to the case record: "He has deliberately tried to undermine the authority of the teachers, is saucy and insubordinate, refuses to obey, and makes fools' of the teachers for the amusement of the other boys. He tries to attract attention by clowning, and tried to make himself out a 'tough guy,' telling such realistic stories about life at the Lyman School that people thought he must have been there. He has been in three foster homes before this school placement, showing the same reaction to authority and discipline in each, and he has particularly evidenced his hatred toward men who tried in the most friendly way to supervise him." He was discharged from the trade school, the day before I saw him, for insubordination and fighting with the masters.

Physical examination showed a good looking, well

developed youngster (above the average in height, and 13 pounds above the average in weight). He had no physical defects or disabilities, and the clinical history revealed that he had never been seriously ill. Two things were noted that were of interest later: he was very proud of his physique (flexing his muscles, expanding his chest), and he was well groomed and clean.

Psychologic examination showed the boy to be of average or better than average intelligence—he had an IQ of 117 on the Terman Test. He showed superior ability in work with concrete material, and hence one would have expected him to do well in trade training. He started school at 5 years, got A's and B's in the grades until his 12th year, when in the 8th grade he lost all interest in school, his marks dropped well below passing and he was not promoted. Inasmuch as most of the difficulties for which he was referred began at that time, one could tentatively say that the precipitating (but by no means causal) factor or factors presented themselves then.

A glance at the family history gave a suggestion of this precipitating factor. Frank was the eldest of three children. His father, although intelligent, was spasmodically employed as a skilled workman, for most of his married life, he had been cruel and abusive to his wife. He had one job after another, having little difficulty in finding work even during the depression years, but reportedly resigned his job at the least sign of authority on the part of his employers. He was thin, suffered from stomach trouble, and was nervous. The mother was described as "intensely neurotic, a poor manager." The home was poorly kept, and the children were allowed to run wild. Three years before I saw the boy, the precipitating event occurred: the home was broken up, a divorce followed, and the boy—after unsuccessful attempts to live first with the mother and then with the father—was taken over by a governmental agency. His four unsuccessful attempts at foster home living followed.

One would expect that this boy with such a background would welcome a good home, with love, security and a chance to gain the academic and vocational training that

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his own home would never allow him to experience. He was bright and attractive. What were some of the reasons for his inability to make an adjustment? Or better—for the purposes of this discussion—what were the conditioning factors in the first 12 years of this boy's life that made him a behavior problem for these 3 years?

The psychiatrist must look beyond the precipitating factors for the evidences of the conditioned responses, and he knows them to be varied, subtle and sometimes vague and symbolic, but he also knows that they are nonetheless effective and powerful. He looks for them principally in the relationships of the boy with each parent in turn, and specifically he seeks those individual traits, characteristics or patterns that the child has taken up from each parent and made a part of his own personality, and conversely he searches for that part of the parent that he rejects and hates. Believing these mechanisms to be couched best in terms of interpersonal relationships, the psychiatrist calls them identifications with or rejections of people or of any of the multivariates attributes of these most important people—the parents. The psychologist, presumably, calls them conditioned responses and inhibitions, and would say that the parents are the unconditioned stimuli that determine a child's response to people beyond the home ever after. Therefore, Frank's attitudes—his loves, hates and fears, and his acceptance or rejection of people—even extending to what Pavlov and Krasnorgorski call "generalization" to the most trivial attributes (the behaviorists would call them "elements") of various persons' faces, hair, clothes, occupations, hobbies and so forth,—all were largely based on his attitudes toward his parents woven into his behavior patterns in his very early years. Some of these points, as given by him to the psychiatrist, are briefly presented below.

In the course of the interviews, the boy gave many descriptions of his father and his feelings of hatred toward him long before the excesses leading to the divorce were in evidence. His father, of course, was the source of discipline in the family and was usually unreasonable in his demands. Moreover, he was more lenient with the other children, and his tendency to take their part in intrasibling rows and quarrels led Frank to develop strong feelings of jealousy of the siblings because of alleged favoritism. Frank particularly emphasized his hatred of his father's personal habits: his father did not keep himself, or his clothes, clean; he was slovenly, did not shave every day, took little or no care of his teeth, and seldom bothered to wear a necktie. The father was thin and withal he was frequently absent from meals, ate a poorly balanced diet, and drank and smoked cigarettes to excess. In brief, then, these are some of the characteristics of the adult man (the stimulus) that prompted responses of obedience from Frank for 12 very important years; many of these promptings were—as is so frequent in the arduous task of growing up—accompanied by (and hence associated with) various amounts of pain and resentment.

One is interested in the responses given by Frank to men other than the father who later asked that rules be followed and that chores be completed—or even to those adults whose interest in Frank was to help him without asking that he himself do anything in return. I must add, too, that during the time this material was

forthcoming he did not consciously associate his likes and dislikes with his father's personal habits or traits.

In the first place, the boy took a dislike to me, his physician, because I smoked and because I wore blue shirts (his father wore blue shirts). (I shall add, however, that I was not without a necktie, and that I was shaven and, I hope, passably clean.) He was quite careful to emphasize what he was not going to do, hoping to avoid any demands that I might wish to make of him.

In his first foster home, he stayed 2 weeks and then ran away. He described the home as dirty, and he stated that the foster father and foster mother "didn't bother to keep themselves clean, let alone the kids." (This accusation was not true.) He refused to do even the simplest and easiest tasks about the house, was arrogant toward the younger children, and bragged of his physical prowess and criminal exploits when he was trying to impress the older ones.

In the next foster home, everything went quite well for some months until the foster family took two other boys to board. Frank immediately accused the foster father of favoring the other two, and of making him do more than his share of the chores. He fought with these boys, would not allow them in his room, and refused to let them read the books that the foster father had previously bought for him. He finally became so surly and aggressive toward this foster father, whom he had previously liked, that he had to be removed.

In his school placement, he again did well for a short period, but soon his old patterns became evident, although at no time, as he later admitted to me, did any of the masters or fellow students initiate the quarrels. He was at a loss for an explanation of the fundamental cause of his antagonisms, but he readily gave what were to him their most outstanding characteristics. He scorned the younger pupils as babies who did not even keep themselves clean. He would not ride in the bus with them. (His siblings were both younger than he.) He fought with one boy continuously because he was "thin and anemic" (Frank always pictured himself as strong and powerful), and because he was "too well liked by the headmaster." One teacher he disliked because he knew he smoked and he suspected him of drinking alcohol. Another master, the athletic instructor, whom one would expect Frank to look up to and emulate, was an anathema because he was redheaded and had a mustache. (His father has reddish hair and a small mustache.) The shop instructor was sloppy in his habits, did not clean his fingernails, and wore blue denim shirts, open at the neck.

In a temporary home placement, the boy carried over his hatred of the school's athletic instructor to his new foster parent, who happened to be a coach in a nearby college. He admitted that he liked this man at first, but after a reprimand for not helping in the household tasks he took a strong dislike to him and consciously equated the two men in personality and attitudes.

One could add many more instances wherein this boy's reactions to people, and particularly to those in authority, were conditioned (sometimes by association to the minutest details of physique and habit) by his responses to and feelings about the first and most impressive authority-stimulus in

his life, his father I have, of course, not commented on his feelings about his mother or the patterns predicated thereon, but they are quite as interesting and instructive

Treatment of this boy entails a long time process of reconditioning. He must, with assistance, gain insight into the varied and subtle ways by which this initial pattern reaction to his parents and sib-

lings is reactivated with such disastrous results in later and other situations entailing adults and children who are not his parents and not his favored siblings—even though they may have a few elements or attributes in common. In the terms of Pavlov, he must learn to differentiate the people who stand before him as stimuli.

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## POST-PARTUM CARE\*

### Preliminary Report of Studies in a Follow-Up Clinic

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POSTNATAL care is not new in the true sense of the word, and yet in years past, the application of this care has been indifferent and, in general, without sufficiently close supervision to be of any value, either to the patient or to the physician.

One of us (C W S), after close supervision of his own private cases for a period of years, has been impressed by the fact that it would be just as practicable to administer this same care to house cases. Prenatal care is now highly developed and specialized. Why should not postnatal care, which is just as important although not so well recognized, be carried out in the same painstaking manner? It is our opinion that insufficient time is devoted to that part of the post partum period when most of the serious, persistent and chronic conditions of the postparturient woman present themselves.

In most postnatal clinics, patients are discharged six weeks after delivery, unless unusual complications are present. This, we believe, is a serious error because, as previously mentioned, many of the conditions that adversely affect the patient's future life occur after this period. Moreover, a follow up of this period furnishes excellent clinical material for the instruction of medical students, interns, residents and junior staff members. Greenhill<sup>1</sup> advocates the follow up of the postnatal patient for one year and predicts that, if as much care is given after delivery as prenatally, untold misery will be avoided—such as cancer of the genital organs, a high incidence of which is found even in well run clinics.

Accordingly, we decided on a program of examining patients routinely six, twelve, twenty-four and forty-eight weeks post partum, and at as many

other times as each case seemed to require. This procedure has been carried out for only a year, and this is therefore merely a preliminary report.

One of the problems was to impress on the patients the value of our follow up of one year. Enlisting the aid of the Social Service Department, we decided on preparing three form letters: the first letter, which was given to the patient while she was in the hospital, explained our plans and made the first appointment (six weeks after delivery); the second letter, which was sent if the patient did not keep her appointment, gave another date, the third letter, which was sent if the other two were disregarded, asked the patient to come to the clinic on the next clinic day. If she then failed to appear, she was removed from our active file. We also enlisted the aid of the Community Nursing Association, which first undertook the follow up work on a basis of trial, however, the results were so successful that the association has undertaken the problem as a regular function for the coming year.

It has been our practice to have the house staff of the previous three months take over the postnatal service for the following three months, supervise the work of the residents and interns, make suggestions and confirm diagnoses. In addition, the third year and fourth year medical students at Boston University School of Medicine attend in the capacity of observers. The advantage of this system is that the same men who treat the patients have the opportunity to follow them in the postnatal period.

The house and district obstetric services of the Massachusetts Memorial Hospitals comprise yearly 700 to 900 patients, of whom about 500 to 600 are delivered in the hospital and 150 to 200 on the district. On discharge, both house and district cases have a routine obstetric summary and physical examination according to a special

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form, which is forwarded to the postnatal clinic and filed with the record. All patients are instructed in routine exercises and also in the daily practice of vinegar douches in an attempt to restore the normal pH of the vagina; furthermore, they are advised to continue taking iron until the first postnatal visit.

Of the 631 house deliveries for 1940, 482, or 76.5 per cent, returned for a total of 1617 visits. These clinics at first averaged about 24 patients a week for a given month, but gradually grew to average as high as 41. For the year,

TABLE 1. *Census of Postnatal Clinic.*

MONTH	NO. OF ADMISSIONS	NO. OF RE-ADMISSIONS	NO. OF NEW PATIENTS	AVERAGE NO. OF PATIENTS PER WEEK
January	98	72	26	24
February	118	96	22	24
March	151	109	42	38
April	125	95	30	31
May	120	69	51	30
June	163	95	68	41
July	117	80	37	39
August	176	116	60	35
September	128	91	37	32
October	190	146	44	36
November	100	68	32	33
December	131	98	33	33
Totals	1617	1135	482	33

the average was 35 patients, the largest number reporting in June and July, possibly owing to summer vacations. Table 1 shows the growth and monthly variation of the clinic.

Subinvolution

Subinvolution was found in 15 cases. The diagnosis was established on the finding of a large boggy uterus, subjective symptoms and bleeding. A uterus that is not contracted below the symphysis at six weeks was considered to be subinvolved, the fact that multiparity influences the uterus being considered. Twelve cases had no associated symptoms. Three cases had associated bleeding, which was not severe. Hot prolonged douches completed the involution in all these cases. The patients were mostly multiparas with large families who obviously were neglectful in obtaining rest and proper hygiene.

Procidentia

Procidentia was found in only 3 cases; of these, 1 was first degree, and 2 were second degree. Since all these patients were in the childbearing period without symptoms, no treatment was considered necessary. It is our opinion that treatment of this condition should be influenced by the severity of the symptoms and the discomfort experienced. Atlee<sup>2</sup> advocates treatment before late years and before more serious trouble sets in if the patient has symptoms. If, after repair, subsequent labors

are well managed and enough time is allowed to elapse after operation, there should be no ill effects.

Retrodisplacement

Retrodisplacement of the uterus was found in 307 cases, or 60 per cent, and of these patients only 28, or 8 per cent, showed symptoms. Manual replacement, with insertion of a pessary, was tried in all cases with symptoms. Those patients in whom the pessary cured the symptoms, but who did not remain symptom free with removal of the pessary, were referred to the Surgical Service for operation. If the uterus returned to its posterior position without symptoms, once the pessary was removed, we did nothing. We do not believe that a uterus should be replaced anteriorly if the patient is symptomless. DeLee and Greenhill<sup>3</sup> state that exercise for uterine replacement, except in the immediate post-partum period, is worthless. This has also been our experience in the clinic.

Lacerations

Cervical lacerations were observed in 174 cases, or 36 per cent: these were divided into 80 unilateral, or 46 per cent, and 94 bilateral, or 54 per cent. Most cases found were in multiparas, and the degree of involvement was proportional to the number of pregnancies.

Erosions

The commonest complication found in the clinic was erosion, with or without endocervicitis. The erosions were classified as slight, moderate or marked, depending on whether a small or large part of the portio or canal was involved. Slight erosions were found in 225 cases, or 44 per cent, moderate erosions in 56 cases, or 12 per cent, and severe erosions in 34 cases, or 7 per cent, for a total of 315 cases, or approximately 63 per cent of all cases examined.

Matthews<sup>4</sup> states that the etiology of these erosions is trauma, with associated infection, and that the commonest organisms are the streptococcus, staphylococcus, gonococcus and colon bacillus. The gonococcus and staphylococcus are the most frequent offenders. Matthews tells how the columnar epithelium, because of the constant stimulation of infection, pushes out into the vaginal portion of the external os, replacing the stratified squamous epithelium common to this area. Hypersecretion of the glandular structures, if these are obstructed, goes on to the formation of nabothian cysts. Therefore, an erosion is not an ulceration but a new formation of glandular tissue. Wollner<sup>5</sup> states that these changes can be produced by unopposed action of estrin. He be-



lieves that endocrine imbalance is responsible for the production of these erosions. Roblee<sup>6</sup> attempts to show that vaginal pH is the cause of these erosions, and that a cervix with a pH of 6.5 to 7.5 shows columnar proliferation. A report of the Central Association of Obstetricians and Gynecologists<sup>9</sup> reveals that birth trauma is the most significant factor in erosion and endocervicitis. Barrett<sup>7</sup> states that cervical injury occurs in the majority of vaginal deliveries, and that, if they do not heal, these lesions favor the future development of chronic endocervicitis and hypertrophy and may be the source of serious pelvic disease. Fulkerson<sup>8</sup> considers the trauma of abortion or labor to be the cause, and believes that the infective organism is seldom the gonococcus.

In the literature, erosion and endocervicitis have been found to be the cause of leukorrhea, backache, occasional menstrual disturbances, urinary symptoms, sterility and a hearing down or dragging sensation in the pelvis. The value of treating these lesions early is emphasized by Matthews,<sup>1</sup> who states that "the new gland tissue may become malignant under certain conditions." He also shows that there is slight difference between the orderly arrangement seen in cystic hyperplasia and endocervicitis and the disorderly arrangement, with embryonal cells, found in true neoplasia. Moench<sup>2</sup> declares that the infected cervix may become a focus in chronic arthritis.

The popular methods of treating these erosions and endocervicitis appear to be by caustics, electrocoagulation, cautery, conization and the Sturmdorf operation. The controversial attitude of older writers is changing gradually, and more recent work tends to support electrocoagulation and conization. Fulkerson<sup>8</sup> states that caustics and antiseptics are only palliatives and rarely curative, and recommends the use of the cautery. Frost<sup>10</sup> advocates electrocoagulation not only of the postpartum cervix but also of the prenatal cervix from the sixth week to the fifth month. Much could be said for and against this statement about the prenatal cervix, but we are in agreement with the statement regarding the postnatal cervix. Miller and Todd<sup>11</sup> advocate conization for the more extensive benign lesions of the cervix and say the conization will completely replace the Sturmdorf operation. Greenhill<sup>1</sup> states that conization will accomplish as much as the Sturmdorf operation without the expense or inconvenience of the latter operation. Stadium<sup>12</sup> condemns cauterization of the cervix because this procedure does not allow microscopic study of the whole or part of the cervical tissue. Zelezny-Baumrucker and Baumrucker<sup>13</sup> are in favor of electrocoagulation to

promote healing and stop leukorrhea. Jacoby<sup>14</sup> states that cauterization with electricity is the method of choice because cervixes heal faster with this than with other methods. Electrosurgery is contraindicated in women in the childbearing age and pregnancy, and in those with acute cervical involvement, and acute and subacute tubal involvement.

In our clinic, we have investigated 100 cases of erosion and mild endocervicitis, which we have coagulated, and 25 cases of marked erosion and endocervicitis with cyst formation, which we have coned.

We believe that some cases of erosion may be due to endocrine influence, but that this complication generally appears late in pregnancy and is completely healed about six weeks post partum. These erosions are often found in the prenatal clinic, and become so severe that the possibility of placenta previa has to be ruled out because of vaginal bleeding. They typically show the heaped-up advance of rapidly proliferating columnar epithelium invading the portio. This picture is consistent with Wollner's<sup>5</sup> theory of "estrogenic stimulation," causing erosion. On discharge two weeks post partum, some cervixes show little evidence of former endocervical hyperplasia, which is consistent with the return of the estrogenic level to normal post partum levels.

The influence of the pH of the vagina in causing and healing these erosions is uncertain. The statement of Roblee<sup>6</sup> that the factor of the lowered pH is the causative agent in erosion cannot be denied or confirmed by our observations. However, that a lowered pH is an essential requisite in the healing of this type of lesion cannot be denied. The spontaneous healing of many mild erosions that exist beyond the immediate post partum period can be explained on these grounds. For this reason, we routinely prescribe acid douches after delivery as an aid in preserving an acid medium.

In agreement with most authors, we believe that the trauma of labor and infection play the leading roles in the causation of these conditions. Of 100 cases selected from our service, we found that the average parity was three and the average time that elapsed before treatment was nine weeks post partum. We believe that the majority of these mild erosions and hyperplastic lesions that are seen in the first six weeks post partum heal spontaneously. For that reason, at the first postnatal visit, we are conservative in our estimation of cervical disease. If an erosion is present, these patients are asked to return weekly for observation. If healing is not prompt, more vigorous therapy

is instituted. In these early cases, caustics, such as silver nitrate, probably have little value. The earliest case that we coagulated was eight weeks in duration, and the oldest was one year. Of these 100 cases, we classified 17 as slight, 50 as moderate, and 23 as marked. Discharge was the chief complaint in 46 per cent, and bleeding, traumatic or otherwise, was encountered in only 5 per cent. No case was coagulated if there was any evidence on bimanual vaginal examination of tenderness suggesting infiltration or other signs of pelvic infection. Twenty of these cases had previously been treated with silver nitrate, some as long as six months. This only helped to convince us of the worthlessness of this method. The average surface-healing time for this series was five weeks. This is much shorter than that reported by Jacoby,<sup>14</sup> unless he refers to complete capillary obliteration. In this series, we had failures in only 2 cases; one, we believe, should have been coned, and the second was not coagulated deep enough but, when recoagulated, healed in six weeks. Four per cent of our patients treated by coagulation became pregnant before they were discharged from the clinic.

There were no cases of activated pelvic inflammation, probably because, as previously mentioned, no case that showed the slightest evidence of pelvic inflammation was coagulated. We have followed 50 cases for three and 17 for six months, with no recurrence.

In the 25 cases of marked erosion and endocervicitis, the therapeutic method of choice was electroconization. The indications for conization, differing from coagulation, were as follows: profuse discharge, uterosacral tenderness, backache attributed to uterosacral infiltration, edema, hyperplasia of the cervix and severe cervical laceration.

Patients were instructed to report for appointment the day that they started menstruating, and to come in to the hospital usually two or three days postmenstrually without breakfast. Pentothal intravenously or nitrous oxide and oxygen was the anesthetic of choice. After coning, the bleeders are coagulated and, if necessary, are sutured. Sutures are also used to reconstruct the cervical canal if extensive plastic measures with the coning knife are necessary. After operation, the cervical canal is packed with iodoform gauze, and the vagina with vaseline gauze. Both packs are left in situ for three days. After removal of both packs, douches are begun daily. If the pH is kept low, there will be less bleeding, and any sutures used will hold better.

The average parity in these cases was four; the time post partum was eighteen weeks. Backache

was found in only 4 cases, about 16 per cent, and we noted that in general the symptom is oftener one of orthopedic than of gynecologic origin. Half the cases showed nabothian-cyst formation—evidence of long-standing infection. One case showed an epithelioma (Grade III), which the pathologist thought was completely removed. The patient was treated with radium and x-ray promptly, and is still under observation. Two cases exhibited polyps that on microscopic examination proved to be benign. The average time required for surface healing was six weeks.

We followed 14 of these 25 cases for three months and 7 for six months. There were no poor results or recurrences, and the patients were free of symptoms on subsequent examination. We encountered bleeding in only 1 case postoperatively; that was two weeks after coning, and the bleeding was probably traumatic in origin.

We have not as yet followed any of these cases through pregnancy, but one of us (C. W. S.) has followed private cases through two or three pregnancies, with no evidence of dystocia or tendency to abortion. There frequently appears to be a narrowing of the cervical lumen at six to eight weeks. This is a simple exuberant proliferation of epithelial cells. At ten to twelve weeks, the same canal is widely patent, owing to recession of the tissues and the disappearance of edema. To date, we have had no cases of stenosis or abortion.

We believe that conization is the therapy of choice in this type of case, but that it should be performed in the hospital under anesthesia, because of the danger of severe bleeding. Furthermore, this procedure allows a thorough examination to be done on the cervix and ample time to destroy all nabothian cysts. The use of excessive current destroys tissue for the pathologist and causes excessive slough, which may be followed by bleeding. Conization is an excellent method of cervical biopsy, by which many cases of unsuspected cancer may be discovered, and it does not cause dystocia or stenosis.

### *Anemia*

Only 2 cases of anemia were encountered post partum; they were both of a dietary nature and responded to diet and iron therapy. This condition may be eliminated if the patient is instructed in taking some type of iron preparation during the first six weeks following delivery and if a proper diet can be followed.

### *Perineal Relaxation*

In the hospital, the use of perineotomy is routine in all primiparas and also in multiparas when

indicated. The benefit of this practice can best be seen in that only 4 cases showed poor perineal support.

Only 2 cases of secondary repair, both in the recent post-partum period, were performed in the hospital. One was especially interesting in that a vitamin C determination showed the patient to have subclinical scurvy. After treatment with vitamin C, the patient was repaired and promptly healed. The other was a case of infection, which broke down.

### *Cystocele and Rectocele*

Slight degrees of cystocele and rectocele were found in many cases. However, only 30 severe cases of cystocele, or 6 per cent, and 21 marked cases of rectocele, or 4 per cent, were discovered. This is a very small number, when one considers that many of these were found in women who had had many pregnancies and who had been delivered at home.

Cystocele and rectocele in slight degree appear to be the end result of almost all deliveries by the vaginal route. We believe that prophylactic forceps delivery and perineotomy as routine procedures greatly reduce the severity of these complications. We also think that great damage may be done to the pelvic tissues, even where there is no external laceration.

### *Infections*

No proved cases of gonorrhea or trichomonal infection were observed, but there were occasional cases of infection by monilia. In consideration of the number of examinations done, this is rather remarkable. Greenhill<sup>1</sup> states that no pathogenic organism except monilia can exist in a medium below a pH of 5.

### *Nonobstetric Diseases*

A very short time had elapsed before we realized that we should find many conditions in these women that would be beyond the scope of our clinic. This required the reference of 137 cases, or 27 per cent, to other clinics for treatment. Appreciating that cases involving the kidneys should be more closely followed than the average patient, we established a close link up with the genitourinary service, and cases were jointly followed in detail. We hope in the future that this study will be a source of information and research, and that lessons of value will be deduced. At the present time, the follow up of this type of case in the remote post partum period seems to be neglected. Table 2 shows the distribution of cases referred to other clinics. Two cases referred to the surgical and genitourinary services are of special interest.

The patient in one case complained of pain in the left lower quadrant for which no apparent cause was found; this was when she was about five months pregnant. The pain became severer when the patient walked or arose from a sitting position, and did not radiate. During the post-partum period, a mass was found in the left

TABLE 2 Cases Referred to Other Clinics

CLINIC	NO. OF CASES
Medical	39
Orthopedic	25
Surgical (House)	13
Prenatal	11
Genitourinary	10
Surgical (Out Patient Department)	8
Eye	8
Thyroid	5
Gynecological	4
Endocrine	4
Cardiac	3
Nose and Throat	3
Skin	3
Vascular	2
Rectal	2
Dialysis	2
Authors	1

upper abdomen. The pain, although not constant, became severer at times. There were no genitourinary or gastrointestinal symptoms or loss of weight. At operation, a large ovoid shaped, moderately movable mass was found; it was 15.2 cm. in length and 8.9 cm. in width, extending from the upper border of the left broad ligament to within 2.5 cm. of the lower pole of the left kidney. The peritoneum over the tumor was thickened and edematous, with the appearance of an inflammatory mass. The mass was found to contain old chocolate colored blood. The diagnosis of a retroperitoneal hematoma was made. The etiology of the hematoma could not be proved, and there was no history of trauma.

The patient in the other case complained of pain in the left hip and left lower quadrant for a year; it had become worse during pregnancy. After delivery, the patient was followed in the post-partum clinic, where a pelvic mass was found. The diagnosis of ectopic kidney was made. The kidney was removed, and the patient made an uneventful recovery.

### SUMMARY AND CONCLUSIONS

Nearly 500 obstetric cases were followed for as long as one year post partum. The results indicate that prolonged and intelligent post partum care is extremely valuable in preventing, discovering and properly treating the sequelae of delivery.

The commonest complication after delivery was erosion, with or without endocervicitis. The causes of the erosions may be divided into endocrine, chemical and traumatic associated with infection. Coagulation and conization are the methods of choice in treating these lesions. The latter is a hospital procedure, and should be performed under

anesthesia. Coagulation and conization should never be done if there is any evidence of pelvic infection.

Rest and proper hygiene are essential for proper involution of the uterus. Retrodisplacement of the uterus, without symptoms, is normal in many cases. If symptoms are found early in the postpartum period, manual replacement and the insertion of a pessary comprise the method of choice for treatment. Surgery may be resorted to if the condition is unrelieved by these methods.

If there are symptoms, procidentia calls for surgery.

Prophylactic forceps delivery and perineotomy, if necessary, prevent much damage to the pelvic tissues.

Cases involving the kidney should have more intensive and specialized follow-up.

Backache is oftener orthopedic than gynecologic.

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MEDICAL PROGRESS

CARDIOLOGY: I. CHEMOTHERAPY IN HEART DISEASE.  
II. THE FALSE DIAGNOSIS OF ORGANIC HEART DISEASE\*

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I. CHEMOTHERAPY IN HEART DISEASE

THE striking therapeutic successes achieved by the sulfonamide compounds in a variety of diseases have led naturally to the trial of these substances in the treatment of various diseases of the cardiovascular system. Sufficient time has elapsed to make it profitable to review and evaluate the results obtained to date in the chemotherapy of heart disease.

Rheumatic Fever

Hopes that the sulfonamide compounds would exert a favorable effect on active rheumatic fever have not materialized.<sup>1,2</sup> As pointed out in a previous communication,<sup>3</sup> convincing studies have demonstrated no beneficial effects on chorea or on active rheumatic infection in any of its stages. On the contrary, the incidence of toxic reactions to these drugs is apparently increased, and the

clinical course of the illness seems to be adversely affected. When patients with rheumatic heart disease suffer from acute streptococcal tonsillitis, conservative clinical judgment must be exercised about the advisability of administering a sulfonamide compound, particularly since it is the impression of some observers that latent rheumatic infection may be activated by such chemotherapy.<sup>1</sup>

Several studies<sup>4-6</sup> have been made to determine whether sulfanilamide administered prophylactically to patients in the latent phase prevents recrudescences of acute rheumatic fever. It is recognized that recurrences and exacerbations are often associated with upper respiratory infections. It therefore seems reasonable that the prevention of hemolytic streptococcus infections may prevent these rheumatic recrudescences. Thomas and her associates<sup>6</sup> have recently reported the results of a four-year study. Sulfanilamide was given continuously from October or November until June to 55 patients with recent histories of acute rheumatic fever during 79 person-seasons between 1936 and 1940. Sixty-seven patients with a similar history who were given no prophylactic treat-

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ment were observed simultaneously during 150 person seasons. Major rheumatic recrudescences did not occur in those receiving sulfanilamide prophylaxis, but major attacks of acute rheumatic fever in 15 patients and the development of subacute bacterial endocarditis in 2, resulting in 4 deaths, occurred in the control group. Twenty grams of sulfanilamide was administered daily, divided into two doses taken twelve hours apart. The toxic effects from this prolonged dosage with sulfanilamide were negligible. Encouraging results from similar prophylactic treatment have recently been reported by Coburn and Moore.<sup>1</sup> Infections of the throat were prevented, and rheumatic recrudescences did not occur. These authors who used somewhat larger daily doses of sulfanilamide, namely 30 to 45 gr., noted toxic symptoms in approximately 10 per cent of the treated subjects. The incidence of rheumatic fever in their group of 184 children over a three year period was less than 1 per cent, whereas the expectancy according to the control group was 35 per cent. After the onset of streptococcal pharyngeal infections, administration of the drug did not prevent rheumatic recrudescences.

These encouraging results offer hope that further studies in larger groups by various investigators will provide the basis for an additional method with which to combat rheumatic fever.

#### *Subacute Bacterial Endocarditis*

Until recently, all treatment of subacute bacterial endocarditis has been considered generally ineffective. The use of the various sulfonamide compounds—either alone or combined with hyperthermia, heparin, radiation or intravenous typhoid paratyphoid vaccine—has naturally aroused wide spread interest. In an evaluation of the results of therapy of this condition, three essential criteria must be satisfied: the diagnosis of endocarditis must be established with reasonable certainty, the incidence of spontaneous recovery must be used as a comparative basis, and variations of the virulence of certain infections from year to year must be considered. That spontaneous remissions of the disease and even recovery may occur is evidenced by the reports of various authorities. The most favorable outlook for spontaneous recovery from subacute bacterial endocarditis is contained in publications by Libman.<sup>8,9</sup> He differentiated the so-called "bacteria free" and "recovery" cases, employing the former term to designate those cases in which the bacteria had disappeared but sequelae were present, and the latter to indicate the disappearance of the infection without any residual clinical evidence except the

valvular defect that might be present. He noted full recovery in about 3 per cent of the patients in the usual form of the disease running a course of four to eighteen months or more. In a later report,<sup>9</sup> Libman enumerated 12 recoveries in a total of 1000 cases. Three per cent probably represents, therefore, the most optimistic incidence of spontaneous recovery. In 200 cases collected from the literature and from the records of the Mt. Sinai Hospital in which the sulfonamide drugs were administered, recovery occurred in 6 per cent.<sup>10</sup> In much smaller groups of cases in which chemotherapy was combined with heparin, hyperthermia or other measures, the recovery rate was somewhat higher. The number of cases was too small, however, to yield conclusive results. In general, it appears that all the combined methods of therapy have as their effective agent the sulfonamide compounds. Indeed, untoward complications such as embolism and cerebral hemorrhage seem somewhat more prevalent in cases treated by the combined methods.<sup>11-13</sup> Present information permits no definite statement regarding the sulfonamide drug of choice. Sulfathiazole, if it is well tolerated, is effective with unusual organisms as well as with *Streptococcus viridans* and nonhemolytic streptococci and is evidently somewhat preferable to sulfanilamide and sulfapyridine. Information regarding the usefulness of sulfadiazine, which has been recently introduced, is meager, but the report by Finland and his associates<sup>14</sup> is not encouraging. They obtained negative blood cultures after treatment in only 1 of 5 cases, in the others, the bacteremia persisted in spite of continued therapy. At the time of their report, 1 patient was still under treatment, the other 4 having died.

The generally disappointing results of chemotherapy in subacute bacterial endocarditis, despite the not infrequent negative blood cultures obtained following administration of the drug, are made understandable by the work of several groups of investigators,<sup>15-17</sup> who have studied the bactericidal effect of the sulfonamides on various strains of streptococci under various conditions of growth in vivo and in vitro. Human blood clots suspended in solutions of sulfanilamide, sulfapyridine, sulfathiazole and sulfamethylthiazole for periods of one to fifteen days do not show any appreciable penetration by the drug. Even in those cases in which the drug is actively bactericidal for the causative organism, the layer of fibrin acts as an impenetrable barrier. As Duncan and Faulkner<sup>17</sup> have pointed out, this does not necessarily signify that complete eradication of the infection is theoretically impossible. In the

course of time, all the pre-existing thrombi could be organized into fibrous scar tissue, and all newly formed thrombi in a patient under active treatment would be impregnated with the drug. The conditions will tend to become less and less favorable for the growth of the organism, if an effective drug is taken continuously for a long time. Subacute bacterial endocarditis, however, is unlike the ordinary infection caused by a hemolytic streptococcus. It is primarily a focus of growing, relatively avirulent streptococci in a fibrinous platelet mass, which not only completely isolates the organisms contained within it from the living tissue of the body, but may also act to prevent them from coming in contact with any particular chemical substance introduced into the blood stream. The small number of reported recoveries is therefore not surprising.

To summarize, the incidence of recovery following the use of sulfonamide therapy warrants its application in cases of subacute bacterial endocarditis, and the earlier the treatment is instituted, the better presumably are the chances for cure.<sup>18</sup> The evidence for increased therapeutic value in combining sulfonamide therapy with other agents is not sufficiently impressive to indicate the use of the latter, particularly since untoward complications may be thereby introduced and may involve additional expense and hardship to the patient. In a large proportion of the cases treated with sulfonamide compounds, blood cultures become negative, and clinical improvement, reflected by lowering of the temperature and heart rate and increased sense of well-being on the part of the patient, may occur only to be followed by relapse. The antipyretic action of some of the sulfonamides must be borne in mind.<sup>19</sup> If one of the sulfonamides is poorly tolerated or is ineffective, one of the other preparations should be utilized. In some patients who recover, not only do the usual clinical signs of activity disappear, but the sedimentation rate returns to normal.<sup>16</sup>

#### *Prophylactic Use of the Sulfonamide Drugs in Relation to Endocarditis*

Many readers will have noted in their own experience—and this impression is further strengthened by case reports in the literature—the association of recent tooth extraction, tonsillectomy or upper respiratory infection with the onset of endocarditis. It is consequently of great interest to note the finding of Fischer and Gottdenker<sup>20</sup> of positive blood cultures within two hours after uncomplicated tonsillectomy in 21 of 64 cases. Blood cultures obtained preoperatively and from

twelve to twenty-four hours after operation were uniformly negative. Of 18 cases in which nasal operations were performed, 2 showed transient bacteremia.

Palmer and Kempf<sup>21</sup> report the presence, usually in pure culture, of *Streptococcus viridans* in more than 90 per cent of extracted teeth from which cultures were taken. They also obtained blood cultures on 82 patients who had dental extractions under local anesthesia; in no case were more than two teeth removed. Negative cultures of the blood were obtained in all immediately before operation, whereas 14 of the 82, or 17 per cent, showed positive blood cultures immediately after the extractions. In 13 of the 14 patients with positive cultures, the blood was sterile ten minutes later. Transient *Streptococcus viridans* bacteremia has been observed after dental extractions by other investigators<sup>22</sup> in approximately the same percentage of cases.

These observations suggest that, in patients with pre-existing rheumatic valvular lesions or congenital defects in the heart, localization of the organisms on the lesions during transient bacteremia may initiate the bacterial endocarditis. The frequency with which sulfapyridine or sulfadiazine produces negative blood cultures in patients with subacute bacterial endocarditis raises the question whether a sulfonamide drug should not be administered before operative procedures in patients who are particularly susceptible to endocarditis, that is, persons with congenital heart disease or healed rheumatic valvular disease with normal rhythm and no signs of congestive failure.

#### *Acute Endocarditis*

Although recovery from simple gonorrheal bacteremia is not uncommon (indeed a transient bacteremia probably occurs in every case of gonococcal arthritis), spontaneous recovery from proved gonococcal endocarditis is extremely rare. Only 3 examples of proved cases with recovery were cited in 1939 by Futcher and Scott.<sup>23</sup> Newman,<sup>24</sup> in 1933, and Davis,<sup>25</sup> in 1940, also reviewed the subject. Since sulfanilamide and the related chemotherapeutic compounds have been shown to be effective in the treatment of gonorrhea, these drugs have been administered to patients with gonococcal endocarditis. The recent reports of such cases, with recovery after treatment with sulfonamide compounds,<sup>23, 26</sup> although not conclusive, warrant further trials of the therapeutic efficacy of these drugs. Acute endocarditis due to staphylococci, meningococci or pneumococci almost invariably results in death, even though bacteremic cases without endocarditis may respond favora-

bly.<sup>14, 27, 28</sup> The earlier the treatment with sulfonamide compounds is begun in these conditions, the more favorable are the chances for recovery.

## II. THE FALSE DIAGNOSIS OF ORGANIC HEART DISEASE

Cases are not uncommon in which the false diagnosis of heart disease has led to serious if not tragic consequences. Such errors are due to the fact that it is usually easier to be certain of organic heart disease on the basis of definite pathologic findings than it is to be certain that no disease is present when the findings are equivocal.<sup>29</sup> Parkinson<sup>30</sup> has called attention to the danger of making a definite diagnosis of heart disease on the basis of such findings, stating, "A shaky sign is a poor foundation for a weighty diagnosis." The induction of thousands into the armed forces has naturally led to increased interest regarding the significance of various symptoms and signs.<sup>31-33</sup> Hence, it seems appropriate to review the significance of the equivocal signs and symptoms of cardiac disease in otherwise normal persons; the effect of pathologic conditions on the heart, such as endocrine disorders and nutritional states, will not be discussed.

### *Sinus Arrhythmia*

The decided phasic slowing of the heart beat with respiration, that is, sinus arrhythmia, may be noted by anxious patients or their relatives. It is usually asymptomatic, occurs particularly at the extremes of life in the young and the aged, and is of no pathologic significance.

### *Bradycardia*

Cardiac rates as low as fifty are found not uncommonly in young athletes; but, in contradistinction to the bradycardia of heart block, the cardiac rate rises in a normal manner on effort. Such observation of the cardiac rate on exercise will usually establish the diagnosis. Similar slowing of the heart may be observed after acute fevers.

### *Premature Contractions*

Premature auricular or ventricular contractions not infrequently lead the apprehensive patient to seek medical advice; the more stolid may be completely unaware of their presence. In the absence of other evidence, these irregularities should not be considered to indicate heart disease, for they may be found in hearts otherwise completely normal. In aging persons previously free of such abnormality, regularly recurring extrasystoles may, however, be an early indication of coronary arteriosclerosis. The etiologic role of coffee, tobacco and

alcohol in these disturbances should always be considered.

### *Paroxysmal Auricular Tachycardia*

Paroxysmal auricular tachycardia, with its abrupt onset and offset, and its absolutely fixed regularity at rates of 150 to 200 or even 240, generally produces severe palpitation, substernal discomfort and great anxiety. It is the commonest and least serious type of paroxysmal heart action and is often present in otherwise normal hearts. In other subjects, paroxysmal auricular tachycardia appearing in the later years may be the first indication of disease of the coronary arteries. Campbell and Elliott,<sup>34</sup> in a recent study of 100 unselected cases, report 3 patients who have lived fifty years after the onset of their paroxysms, another 18 for more than twenty years, and another 26, making 47 per cent, for more than ten years. Although approximately half the attacks are abruptly terminated by pressure over the carotid sinus, in others the paroxysm may persist and lead after many hours or days, if untreated, to congestive failure or cardiac pain. The treatment of this condition has been outlined in a previous report.<sup>35</sup>

### *Paroxysmal Auricular Fibrillation*

Paroxysmal auricular fibrillation may occur in an otherwise normal heart as a manifestation of thyrotoxicosis, as well as in some persons without any disease. In the absence of demonstrable heart disease, particularly in older subjects, the possibility of a pathologic basis for the disorder must be considered. The report of observations by Willius and Dry<sup>36</sup> on 70 patients with auricular fibrillation but without demonstrable heart disease by clinical, radiographic or electrocardiographic studies indicates benignity of auricular fibrillation under such circumstances, and is in accord with the earlier observations of Orgain, Wolff and White.<sup>37</sup> The latter concluded that paroxysms of auricular fibrillation or of auricular flutter are in some persons merely exaggerated functional disorders of the heart, no more indicative of cardiac disease or of a poor prognosis than premature beats or paroxysmal auricular tachycardia.

### *Paroxysmal Bundle-Branch Block*

Electrocardiographic evidence of bundle-branch block generally signifies organic heart disease and, when present in high degree, must be regarded as indicative of serious heart disease. It is therefore essential to recall that bundle-branch block may occasionally be found as part of the Wolff-Parkinson-White syndrome in young or even older healthy persons. This syndrome is characterized by three important features: a short PR interval of

fully studied group of 100 proved cases.<sup>42</sup> Conversely, slight changes in electrocardiographic tracings occur in a significant proportion of persons of this age group in the absence of angina pectoris.<sup>44</sup>

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CASE RECORDS OF THE  
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

## CASE 27461

## PRESENTATION OF CASE

A fifty-one-year-old Greek bootblack entered the hospital complaining of pain in the right hip.

One year before admission, the patient developed a dull ache in the right hip; it was noticeable only when he was standing. He attributed the pain to a right inguinal hernia, for which he had been wearing a truss. Six months passed, and the patient's discomfort reached a point where he was forced to stop working. He walked with a limp, and the pain radiated from the iliac crest down the outer aspect of his leg. It was greatly aggravated by weight bearing and relieved almost instantly by lying down. Because his physician suspected a focus of infection, all the patient's teeth were extracted; but the pain continued, and three weeks before admission it was no longer relieved by lying down. At this time, he noticed a weakness in his right leg, which often became tired and numb. In addition, he developed urinary frequency and nocturia (once a night). He had lost 10 pounds in the preceding six months.

The past and family histories were irrelevant.

On examination, the patient was well developed and nourished and in no apparent distress. He was edentulous. The heart was slightly enlarged, and there was a soft systolic murmur at the base. Examination of the lungs was negative. There was a slight fullness of the right side of the abdomen, and a right indirect inguinal hernia. Moderate tenderness and fullness were present in the right sacroiliac region. Examination of the nervous system was negative except that the left knee jerk was slightly more active than the right. Rectal examination was negative.

The temperature, pulse and respirations were normal; the blood pressure was 132 systolic, 80 diastolic.

Examination of the urine was negative, and no Bence-Jones protein could be demonstrated. A phenolsulfonephthalein test was normal. Examination of the blood showed a red-cell count of 5,700,000 with a hemoglobin of 102 per cent, and a white-cell count of 7600. The corrected sedimentation rate was 13 mm., and the hematocrit reading 50 per cent. The nonprotein nitrogen of

the blood serum was 31 mg., the serum proteins 6.4 gm., the calcium 13.5 mg., and the phosphorus 2.58 mg. per 100 cc.; the phosphatase was 5.5 Bodansky units. A blood Hinton reaction was negative. Examination of the stools was negative.

X-ray study of the pelvis showed a large multilobular defect involving the medial half of the right ilium. The outline of the defect was irregular but well defined, and the cortex was destroyed in several places. A questionable soft-tissue mass was visible in the region of the ischial spine. Multiple septums were visible within the area of destruction. Films of the extremities and chest were negative. An x-ray film of the skull showed two rounded areas of decalcification that were considered to be venous lakes. A chest plate was negative. An intravenous pyelogram showed prompt excretion on both sides. The kidney pelves were not completely visible because of overlying gas. There was no definite evidence of renal disease.

On the eleventh hospital day, an exploration of the neck for a parathyroid tumor was performed. The left lower and both upper parathyroid glands were found and appeared normal. The right lower gland could not be identified.

## DIFFERENTIAL DIAGNOSIS

DR. JOSEPH C. AUB\*: The blood calcium was at a high level; the blood phosphorus was low. This x-ray film of the pelvis gives a different impression from what I expected from reading the report. The periosteum of the ilium shows a complete break. It looks to me as if there were a large tumor there, and the rest of the bones look quite normal. Is there a film of the hand?

DR. AUBREY O. HAMPTON: No.

DR. AUB: This picture will influence me considerably, for hyperparathyroid lesions of bones do not cause destruction of the periosteum, and malignant tumors, of course, are associated with such destruction.

DR. HAMPTON: In this pyelogram, I cannot see anything in the kidneys. The kidney outlines and pelves are normal. I am not imagining all this, in spite of the fact that the films are poor. I think you can see that the kidneys are fairly normal.

DR. AUB: Here is a man who had a tumor mass in his pelvis, with no other abnormality on x-ray study. The bones look quite well; there is no evidence of the characteristic osteoporosis of the hyperparathyroid state. The blood calcium was

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high, the blood phosphorus low, and the total protein normal; no Bence-Jones bodies were found in the urine. I am surprised at the tumor mass. I do not like this lesion. It does not look like one due to hyperparathyroid disease, but I probably should have advised operation just as others did.

Then the question arises whether this patient had a parathyroid tumor deep in the chest. The lower parathyroid glands may go down in the chest along with the thymus; I assume that at operation the upper part of the chest was explored.

I see that Dr. Albright wants to say something. Do you want to help me, Dr. Albright?

DR. FULLER ALBRIGHT: No; I want to hinder you. I see that Dr. Hampton is putting up more films. I do not want him to show you too much.

DR. AUB: All right. I assume that the chest was explored, but one cannot always find parathyroid tumors situated down in the chest simply by exploration from a neck incision: one has to open the chest to explore properly.

The reason one would be so anxious to find a parathyroid tumor in this patient is not that the blood calcium was high, but that the blood phosphorus was low. Most patients with osteoclastic tumors have a normal blood phosphorus, although they may have a high blood calcium—as high as 15 or 16 mg. per 100 cc.

What is the differential diagnosis? It is obviously hyperparathyroidism, multiple myeloma, hypernephroma or a carcinoma of the breast, which is very rare in men. The diagnosis of prostatic tumor is much less likely because the metastases of this tumor are not osteoclastic. I rule out myeloma because the high blood calcium in multiple myeloma is practically always associated with high total protein in the blood stream, which was not found in this patient. I rule out breast tumor because it is not reported in the record. I rule out prostatic tumor simply because it does not look like it. Might I ask if exploration of the upper mediastinum was done?

DR. ALBRIGHT: It was done from above. They went down as far as they could but did not feel anything.

DR. AUB: When I first read the report, my diagnosis was hyperparathyroidism, with tumor in the mediastinum, and my second choice was hypernephroma, in spite of the negative urine and in spite of the x-ray examinations that were reported negative. Now that I see the x-ray films,

I really think the kidney shadows do not stand out well.

DR. HAMPTON: Here are two more films taken at the same time. They are not much better. They have the same general appearance.

DR. AUB: Do they satisfy you?

DR. HAMPTON: No; they are unsatisfactory. I think you are correct in saying that the examination was poor.

DR. AUB: The x-ray appearance of the pelvis looks as though it were due to a malignant tumor, whereas the chemical analyses are proper for hyperparathyroidism. Then there is the problem of the soft-tissue mass and also of the weakness in the leg, which implies peripheral-nerve involvement. Largely on the basis of the x-ray films, I am going to make a diagnosis of malignant tumor and not of parathyroid tumor situated in the mediastinum. I did not plan to make that diagnosis when I came here. If I were in charge of the case, what I should propose doing next would be to take a biopsy of the tumor in the bone, before recommending the second operation of cutting the sternum and looking in the upper mediastinum. The most likely diagnosis of the malignant tumor would be a hypernephroma in spite of the normal urine, because it is the most probable malignant osteoclastic tumor.

DR. HAMPTON: This kidney pelvis does appear to have a defect in the superior margin.

DR. ALBRIGHT: We were influenced by another case we had seen before, which I thought was a dead ringer for the case under discussion. That patient had also had pain in the hip, and the roentgenogram demonstrated a lesion in the ilium very similar to the one in this case. Dr. J. H. Means was asked to see the other patient in consultation, and he considered diagnoses of multiple myeloma and hyperparathyroidism, and ordered serum calcium and phosphorus determinations, as well as a search for Bence-Jones protein in the urine. The serum calcium was high, 13 mg., and the serum phosphorus low, 2.0 mg.; small amounts of what was thought to be Bence-Jones protein were found. Accordingly, the consultation was not much help. Some of us thought that the patient had hyperparathyroidism; others considered multiple myeloma. We decided to biopsy the lesion; both sides were apparently wrong. He had an enchondroma, which was removed. The Bence-Jones proteinuria disappeared, but the hypercalcemia persisted. At a somewhat later date, the parathyroid glands were explored, and the

diagnosis of hyperparathyroidism was substantiated.

DR. HAMPTON: I should like to disagree with Dr. Albright. The two cases are not entirely similar. The cortex of the bone is destroyed in the present case, and intact in the other.

DR. ALBRIGHT: Why could not a benign tumor destroy the cortex?

DR. HAMPTON: It expands but does not destroy it, because bone destruction is due to vascular pulsation rather than to tumor invasion.

DR. TRACY B. MALLORY: The next step was what Dr. Aub said that he would advise—a biopsy of the tumor of the ilium. That was done and showed obvious hypernephroma. At that stage, they began to have doubts about the intravenous pyelogram, and a retrograde film was taken, which Dr. Hampton will now show us.

DR. HAMPTON: I might point out that this is the third case within a month in which a serious error has been made by relying on the intravenous pyelogram when a retrograde pyelogram would have told the story. The retrograde pyelogram shows a definite filling defect in the upper calyces. I think it is true, however, that the kidney presented a normal outline on its lateral surface. If we had taken a lateral view and demonstrated the kidney, we should have seen the mass in front of or behind the kidney. This case misled us because a hypernephroma ordinarily presents on the lateral margin.

DR. ALBRIGHT: Why a person should have a high serum calcium and a low serum phosphorus when the cause of the disturbance is a tumor destroying bone is an interesting theoretical question. We treated this case by radiation of the tumor masses; the serum calcium went down to normal, and the serum phosphorus went up to normal. Gradually, both values became abnormal again. I suspected that the tumor might be producing parathyroid hormone. I therefore had it assayed by Dr. J. B. Collip, but no hormone was found.

#### CLINICAL DIAGNOSIS

Hypernephroma, with metastases to right ilium

#### DR. AUB'S DIAGNOSIS

Hypernephroma, with metastases to bone

#### ANATOMICAL DIAGNOSES

Hypernephroma of right kidney, with metastases to right ilium, fifth lumbar vertebra, sacrum and left ilium.

Bronchopneumonia.

Arteriosclerosis, coronary, slight.

Emaciation

Decubitus ulcer.

Operative scar: parathyroid exploration

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This patient survived nearly three years, and finally died and came to autopsy. He was found to have a still fairly small hypernephroma of the right kidney but a large tumor involving most of the right side of the pelvis. The fifth lumbar vertebra, the sacroiliac joint, a good deal of the sacrum, and the symphysis pubis had all been destroyed by direct invasion.

DR. AUB: Were there any other metastases to the bones?

DR. MALLORY: Neither grossly nor microscopically. A good deal of the bone marrow was aplastic, almost certainly as the result of x-radiation, although there were foci of moderate hyperplasia.

DR. OLIVER COPE: What was the cause of death—intercurrent infection?

DR. ALBRIGHT: The patient got weaker and weaker, and died.

A PHYSICIAN: Did they find the other parathyroid gland?

DR. MALLORY: At autopsy, yes. It was not neoplastic.

DR. AUB: It was normal?

DR. MALLORY: Yes.

#### CASE 27462

#### PRESENTATION OF CASE

A seventy six-year-old man was admitted to the hospital because of severe abdominal pain of four to five hours' duration.

Eight months before entry, he had a brief bout of abdominal cramps lasting about ten minutes. Three weeks before admission, he experienced a similar episode, which responded well to a little whiskey. The patient stated that he began to have pain in the umbilical region two days before coming to the hospital. His relatives, however, who seemed to have watched him closely, were sure that he had been quite well until early on the morning of admission. At this time, he was found groaning from severe abdominal pain, which centered about his umbilicus. A local physician thought that the patient had a perforated ulcer, gave him morphine, and sent him to the hospital.

The patient had practically always enjoyed good health. His weight had been constant for some

time, his appetite was good, and his bowels had been regular, with no recent change in habits or in the character of the stools. Twenty-five years before entry, he had "stomach ulcers," which disappeared within several weeks after treatment of unknown variety. One of his daughters had died of "pelvic cancer."

On examination, the patient was an elderly, slender man with dry, pale skin; he was groaning from pain. His abdomen was convex, tympanitic and tense, with considerable voluntary spasm. There was marked tenderness, most pronounced in the periumbilical region and right lower quadrant. No masses or hernias were present. The heart and lungs were not remarkable. The right eye was blind because of a cataract.

The temperature was 102.4°F., the pulse 104, and the respirations 34. The blood pressure was 130 systolic, 75 diastolic.

Examination of the blood showed a red-cell count of 4,200,000, and a white-cell count of 12,500 with 5 per cent mature polymorphonuclears and 80 per cent immature polymorphonuclears.

A flat roentgenogram of the abdomen showed a large quantity of air beneath both sides of the diaphragm. No dilated loops of small bowel were visible.

Aspiration of the abdomen gave thin, slightly milky fluid. Culture of this fluid grew colon bacilli and hemolytic streptococci.

Exploratory laparotomy was performed under local anesthesia on the morning of entry.

#### DIFFERENTIAL DIAGNOSIS

DR. HENRY FAXON: Does the x-ray film add anything?

DR. JAMES R. LINGLEY: No; it just shows the air beneath the diaphragm, as described.

DR. FAXON: Does it show dilatation of the large bowel?

DR. LINGLEY: No.

DR. FAXON: Any of the small bowel?

DR. LINGLEY: No.

DR. FAXON: The salient features of this case are that the patient was an elderly man, apparently in previous good health, who suddenly developed an acute condition of the abdomen, with a large amount of free gas beneath both diaphragms. He obviously had a peritonitis, and the most arresting single finding was the presence of this gas.

Such collections of subphrenic gas may arise from three main sources. The first is the introduction of air by perforation of the abdominal

wall or diaphragm by trauma or surgery. The history in this case makes it certain that air was not introduced into the peritoneal cavity from without.

The second cause of gas beneath the diaphragm is peritoneal infection with gas-forming organisms. However, if it had been infection in the peritoneal cavity, with the secondary formation of gas, one would expect a longer story and localization of the process beneath the diaphragm on but one side.

The third cause of such gas is the perforation of a hollow viscus, which seems the most likely explanation in this case. Such a perforation could come about in one of two ways—secondary either to an obstruction of such severity that the bowel ruptured or to erosion through a localized ulcerative area. If it were due primarily to obstruction, it would certainly seem that this patient should have had a longer story. The episodes of abdominal cramps referred to in the history eight months and again three weeks before seem to me of too short duration to have any real significance on this basis. I can hardly believe that they represented temporary obstruction that straightened out, although conceivably they might have been due to a volvulus of the colon. Such a condition is common in men and in elderly people, and might have gone on to the point of actually causing perforation in the attack that brought the patient to the hospital, but that seems extremely unlikely.

The perforation of the hollow viscus must have been due to erosion of some actual lesion through the wall of the gastrointestinal tract. Of such lesions, one possibility would be cancer, but it seems to me that with cancer of the rectum or sigmoid the patient would have had either some change in bowel habit or blood in his stools, during the recent past. Had he had a malignant lesion of the right colon, he might well have had very few symptoms, but it would be extremely rare for such a lesion to go on to the point of perforation with a red-cell count of 4,200,000. Lymphoma is another possibility, for the fluid they aspirated from the abdominal cavity was milky and much more consistent with such a diagnosis than with perforation of the colon.

The pain was chiefly periumbilical and in the right lower quadrant, which suggests that this was referred from the region of the terminal ileum, appendix or cecum. The patient might have had acute appendicitis, with an abscess that ruptured, for we know that in elderly patients the story is often atypical. The reference of pain would have been quite in keeping with this diagnosis, and

the fact that no mass was felt means but little, for the abdomen was apparently so tender and distended that I doubt if a mass could have been made out at the time of entry. However, I have never heard of a rupture of an appendix that caused the escape of so much free gas in the peritoneal cavity that could be demonstrated beneath both diaphragms.

Diverticulitis is another lesion of the bowel that could perforate; it is not usually associated with bleeding by rectum or anemia, does not give rise to many antecedent symptoms, and can perforate with the escape of gas in the peritoneal cavity. However, the signs and symptoms of diverticulitis are characteristically in the left lower quadrant, whereas it seems to me that in this case the localization of the pain was too much on the right side to make diverticulitis seem likely.

The doctor who referred the patient here sent him in with a diagnosis of perforated ulcer, which, despite certain definite objections, seems to me the most likely diagnosis. A perforated ulcer is one of the few lesions that give rise to the escape of such a large amount of gas. Such a lesion might well cause gas beneath both diaphragms, furthermore, with the obliquity of the attachment of the mesentery, the gastric fluid as it gravitated downward would give rise to pain more on the right than on the left side. The ulcer story of the past is so vague that it means but little. I am distinctly surprised that colon bacilli were cultured when the perforation was only four or five hours old. My final diagnosis is peritonitis due to dissemination of intestinal contents from erosion through the gastrointestinal tract, most probably perforation of a peptic ulcer.

DR ROBERT LINTON: Did Dr Faxon include carcinoma as a possibility?

DR FAXON: Carcinoma of the stomach is certainly a good possibility, but if the lesions had been malignant, the patient would probably not have been in such good health up to the time of entry.

DR ALLEN G. BRAILEY. What about ulcer of a Meckel's diverticulum?

DR FAXON. I think it would be extremely unlikely for a patient to show the first symptoms and suffer a perforation of a Meckel's diverticulum at the advanced age of seventy-six. Periumbilical pain would be quite in keeping with a Meckel's diverticulum that had gone on to the point of perforation, but I should not have expected the gas seen under the diaphragm to have occurred unless in the x-ray plate there were signs of small-

bowel obstruction behind the Meckel's diverticulum.

DR ARTHUR W ALLEN: Are you not worried about the story of periumbilical pain of two days' duration?

DR FAXON: I am very much worried about it. When I first read over this case, I thought the patient certainly had a perforated ulcer, but the more I studied it the more I worried over the atypical localization of the pain.

DR ALLEN: I think they should tell you whether the fluid had an odor to it.

DR FAXON: I hoped that they might.

DR TRACY B. MALLORY: Dr Ulfelder, will you tell us about that?

DR HOWARD ULFELDER: Our differential diagnosis ran much like Dr Faxon's but we never seriously entertained a diagnosis other than that of perforated ulcer. His condition was good preoperatively. We operated under local anesthesia through a right upper-quadrant paramedian incision. On opening the abdomen, we found free, nonodorous milky fluid that seemed to come from the right gutter. Exploration of the duodenum and stomach anteriorly revealed no evidence of perforation or disease. We opened the mesocolon below the stomach and explored the lesser cavity, the posterior aspect of the stomach and the duodenum, and still found no cause for the disease. We then turned our attention to the right gutter and, in tracing down into the pelvis, were suddenly greeted with a gush of foul-smelling, thin fluid. His condition became much worse. We believed that the patient had a perforation of the large bowel, of unknown cause. No further surgery was attempted, since the blood pressure dropped so low that it could not be measured. The wound was closed without drainage, and the patient was sent back to the ward for a futile attempt at conservative therapy.

#### CLINICAL DIAGNOSIS

Perforated peptic ulcer

#### DR FAXON'S DIAGNOSES

Perforated peptic ulcer

General peritonitis

#### ANATOMICAL DIAGNOSES

Carcinoma of sigmoid, with perforation

Diverticulosis of sigmoid

Peritoneal abscess, pelvic

Peritonitis, acute, generalized

Pneumoperitoneum

Laparotomy

Prostatic hyperplasia

## PATHOLOGICAL DISCUSSION

DR. MALLORY: At autopsy, we found in the large bowel a number of diverticula. At first, we were suspicious that one of these had ruptured, but they all seemed intact. Finally, just at the rectosigmoid junction, we found a carcinoma with a deeply penetrating central ulceration that had perforated into the abdominal cavity just above the pelvic floor. There an abscess had formed and had evidently been present for some

time, since there was dense fibrinopurulent exudate over all the viscera in this area. In the upper abdomen, there was a generalized milder and evidently more recent peritonitis. I should think that the perforation of the carcinoma and the formation of the pelvic abscess preceded entry to the hospital by a number of days, and that the acute symptoms probably represented a rupture of that abscess into the general peritoneal cavity. Why the pain was periumbilical, I cannot say.

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## APPROVING AUTHORITY

THE attention of the members of the Massachusetts Medical Society is directed to a letter and enclosures that have been received by the Secretary from Dr. Stephen Rushmore, chairman of the Massachusetts Approving Authority for Colleges and Medical Schools. This correspondence should make for a better understanding of a matter that provoked considerable discussion at the October 1 meeting of the Council.

Much dissatisfaction, of late years, has been expressed with the Massachusetts Medical Practice Act. It has been described as archaic and most certainly not in keeping with the advances in the science of medicine. As the result of this dissatisfaction, the act was amended in 1936 to create an approving authority in whose hands would be

the power to set up minimum standards for colleges and medical schools that must be met if the graduates of these colleges and medical schools were to be permitted to take the examinations offered by the Massachusetts Board of Registration in Medicine. The amended law provided that the initiative in seeking the approval of this authority must come from the school whose graduates wish to be licensed in Massachusetts.

In the same session of the Legislature, this act was further amended on the advice of Governor Curley. When the bill was presented to the Governor for his approval, he said that he was very much in favor of the thought behind it. He believed, however, that because the decisions of the Approving Authority might involve the property rights of certain individuals,—owners of schools and students whose education represented property rights,—the bill should provide for a review of certain of the decisions of the Approving Authority by a judge of the Superior Court. He added that the property rights of the individual are guaranteed by the Constitution and that the open recognition of this principle in the bill would add strength to the bill itself.

The bill went back to the Legislature and was amended to incorporate this suggestion of the Governor. While it was taking this second trip through the Legislature, it was still further amended to postpone the date of its operation until 1939. The proponents of the bill accepted this latter amendment because it was pointed out that if this bill became effective immediately, certain schools and certain individuals who had matriculated in those schools in good faith might be seriously affected. The thought that some schools should be afforded reasonable time to improve their standards had considerable appeal to the legislators.

The law was again amended in 1938 to extend further its date of operation. The language of this latter amendment is contained in Chapter 247, Acts of 1936, Section 3, as amended. Dr. Rushmore's letter quotes this section. It is particularly referred to here because it does seem to clarify a matter that was discussed at length at

the October 1 meeting of the Council, when the President and Secretary were directed "to give their attention to this matter with a view of enlightening the Council as to what the situation is."

The situation may be briefly stated as follows: an approving authority for colleges and medical schools is now functioning in Massachusetts. This authority has already inspected all medical schools in Massachusetts that have requested inspection and has approved three of these. The initiative for such an inspection must come from the college or medical school. Certain decisions of the Approving Authority are subject to a review by a judge of the Superior Court, sitting in Suffolk County.

Applicants who matriculated in a medical school previous to January 1, 1941, cannot be barred from taking the examination for licensure in Massachusetts even though the school from which they graduated has not been endorsed by the Approving Authority at the time of graduation.

## THE SCHOOL-LUNCH PROBLEM IN BOSTON

IN the September 18 issue of the *Journal*, an editorial commented on the nutritional deficiencies commonly found in American diets and on the consequent importance of the school lunch for children. Since then, a report by the Advisory Committee on School Hygiene,\* dated April, 1940, and dealing with the school-lunch problem as it exists in Boston, has been received. The recommendations in the report are so significant that they are quoted in full:

(1) The situation regarding school lunches for pupils in the public schools of Boston presents problems worthy of careful and prompt consideration by the School Committee.

(2) A thorough reorganization of the system of providing lunches for the pupils is urgently needed.

(3) To accomplish this result, responsibility for the management of the cafeterias in all the public schools of Boston should be placed in the hands of a single director.

(4) Besides the fundamental requirement of high character and organizing ability, the director should have excellent training in and a thorough knowledge of nutrition, as well as training and experience in lunchroom management and the preparation of attractive, palatable food. The appointment of such an individual will require careful consideration. The professional qualifications required for work of this kind have been studied by the American Dietetic Association and the American Home Economics Association.

(5) The functions of the proposed director should include the purchase of food and the supervision of menus, as well as the management of the cafeterias. The qualifications for lunchroom managers should be carefully drawn up, so that efficient workers may be obtained.

(6) The director should endeavor to exemplify in the lunchrooms the dietetic and hygienic principles taught in the schools.

(7) The sale of undesirable foods, such as candy and tonic, in the cafeterias or on the school premises should be stopped. The school children should not be allowed to leave the school premises during the lunch hour, and sales of candy or food to them by outside persons should be discouraged as far as possible.

(8) In some, if not in all the schools, more time should be allowed for lunch.

(9) In some of the schools, the lunch program will require improved cafeteria facilities, more equipment, and better hand-washing facilities and more soap and towels.

(10) Adequate reorganization demands replacement of unqualified cafeteria managers by suitably trained personnel. These should have faculty standing in order that they may be in a position to confer with the school administrators, teaching staff and school health group on common problems of nutrition education.

(11) The director should exercise authority not only over all the cafeterias in the schools, in so far as they serve the children, but also over the following additional activities: food service to nutrition classes; distribution of milk and other foods; and lunches served to teachers or others, if any.

These recommendations received favorable action by the School Committee, and money was recently appropriated to pay the salary of such a director. The Civil Service Commission, in accordance with law, has circulated a notice of an examination to be taken, on November 22, by applicants for the position of "Supervisor of School Lunches."

\*This committee is an official body appointed by the School Committee of Boston. The report was presented to the School Committee after having been approved by the Director of School Hygiene.



As stated in the notice, the duties of the supervisor are as follows

To draw up specifications for the purchase of food supplies, to standardize recipes for the school lunch rooms, to plan menus based upon adequate nutrition standards, to have supervision of all menus, of the direction and preparation of school lunches, of the distribution of milk and other supplies and of lunch room sanitation, to analyze equipment on hand in the lunchrooms and recommend redistribution to develop nutrition education through correction with the health education program, and to perform related work as required

A knowledge of cost accounting is necessary

Applicants must have executive ability adequate to meet organization requirements for the establishment of a city wide lunch system, and ability to work with and to direct the work of others

This new office will be a position of prime importance for the health of Boston's school children. All persons interested in their welfare will recognize that the children should receive school lunches, at minimum cost, that compare favorably with those provided by other forward looking communities

Unfortunately, certain conditions raise a question concerning the adequacy of the provisions for obtaining a properly qualified person. Firstly, regulations require that applicants be citizens domiciled in the State at least a year and in Boston at least six months. Since a school lunch system of this scope is nonexistent in Massachusetts, this provision limits the examinees to persons having comparatively little experience. Secondly, the General Laws provide for veterans preference among applicants passing with grades above 70 per cent. Thirdly, the salary is less than those paid to the holders of similar positions in cities smaller than Boston. And, finally, there is no limitation concerning age. It is hoped that the written examination will be so inclusive and the physical examination so thorough that they can be passed only by persons who are adequately trained and physically fitted to perform the important and arduous duties of the new office.

## MEDICAL EPONYM

### LANDRY'S PARALYSIS

Dr Jean Baptiste Octave Landry (1826-1865) published "Note sur la paralysie ascendante aigue [Note on Acute Ascending Paralysis]" in the *Gazette hebdomadaire de medecine et de chirurgie* (Paris) (6: 472-474 and 486-488, 1859). A portion of the translation follows

The object of this note is to call attention to a morbid condition that is rather uncommon and generally unknown but deserves a place among the most remarkable diseases in the pathological category

In these cases, the symptoms, beginning in the extremities, successively involve the upper portions of the body, those more central relatively to the nervous system becoming gradually augmented in intensity in the invaded organs. These symptoms frequently tend to become general, and then produce a definite *general paralysis* with all the characteristics of that of the insane

I simply add that, nearly always slowly progressive, it occasionally runs a very rapid course, and may become serious or even fatal in a very short time. It is this variety that I propose to designate *ascending* or *acute centripetal paralysis*

R W B

## MASSACHUSETTS MEDICAL SOCIETY

### APPROVING AUTHORITY

The following letter and enclosures were recently received from Dr Stephen Rushmore, chairman of the Approving Authority for Colleges and Medical Schools, and are reprinted for the information of the members of the Massachusetts Medical Society

MICHAEL A. TIGHE, *Secretary*

\* \* \*

Dear Dr Tighe

In reply to your letter of inquiry on the part of the Massachusetts Medical Society as to the work of the Approving Authority for Colleges and Medical Schools, I regret that the nature of our work precludes the giving out of full details since so much of the information which comes to us may properly be regarded as confidential.

I may say, however, that, under the statute, the inactive rests with the institution seeking approval, and that the Approving Authority has inspected all the medical schools in Massachusetts that have requested inspection. Following inspection, the Approving Authority has approved the medical schools of Boston University, Harvard University and Tufts College.

Attention should be called to the fact that no applicant for examination for registration as a physician may be

rejected by the Board of Registration in Medicine as a graduate of a nonapproved school until 1945. Chapter 247, Acts of 1936, Section 3 (as amended), reads as follows:

The provisions of said section two of said chapter one hundred and twelve as existing immediately prior to January first, nineteen hundred and forty-one, shall continue to govern as to the eligibility of any applicant for registration as a qualified physician who shall have matriculated prior to said date in any legally chartered medical school having power to confer degrees in medicine, but subject, however, to the provisions of section two of chapter one hundred and seventy-one of the acts of nineteen hundred and thirty-three.

Attention should be called also to the fact that the statute specifies that one of the conditions of eligibility for examination by the Board of Registration in Medicine is that the candidate "has received the degree of Doctor of Medicine . . . from a legally chartered medical school . . . approved by the Approving Authority. . . ." Presumably, this means approved by the Approving Authority at the time when the degree was conferred.

I enclose a copy of the "Requirements for Approval of Colleges, Universities and Medical Schools," published in 1936 by the direction of the statute, and a copy of Section 2, Chapter 112, of the General Laws as most recently amended.

The statute of 1936, as amended in 1938, thus gave medical schools nearly five years in which to meet the requirements published in 1936 before inspection with effective approval or nonapproval could occur.

STEPHEN RUSHMORE, M.D., *Chairman*

State House  
Boston

#### REQUIREMENTS FOR APPROVAL OF COLLEGES, UNIVERSITIES AND MEDICAL SCHOOLS

##### *Qualifications Required for Approval of a College or University as Giving Two Years of Premedical Collegiate Work, including Physics, Chemistry and Biology*

The institution will be approved if it has already been approved by the Association of American Universities or the Regional Association of Colleges and Secondary Schools in the territory in which the institution is located.

Since approval by the above-noted organizations may be lacking because it has not been sought or has been refused, and since an educational institution should be judged by its objectives and its adequacy in attaining these objectives, specific requirements may present considerable variation. The following general requirements have, however, been established:

(1) The curriculum should presuppose educational qualifications required for graduation from a public high school as a condition for entrance to the institution.

(2) The instruction should be at the collegiate level generally required of institutions giving similar curricula in the regional group.

(3) Since the teacher is the heart of an educational institution, the competence of the faculty, the organization of the faculty, the working conditions for the faculty and the quality of the instruction will receive special attention.

(4) The physical facilities, including library, must be adequate for the objectives of the institution.

(5) The administrative organization and personnel should be adequate for accomplishing the objectives of the institution.

(6) The institution should provide evidence of financial resources adequate for and effectively applied to the support of its educational program.

##### *Qualifications Required for Approval of a Medical School*

The minimum requirements for an approved medical school as set by the statute and by ruling of the Approving Authority under the statute are as follows:

(1) The school must be legally chartered.

(2) If the school confers degrees in medicine, the school must be legally empowered to confer degrees in medicine.

(3) If the school confers degrees in medicine, the school must see to it that the statutory conditions are fulfilled, namely, that the candidate shall have taken a course of at least four years of not less than thirty-two weeks in each year before the degree is conferred.

(4) If the power of the school to confer degrees is restricted under the charter, the degrees conferred must be under the restriction of the charter.

(5) The school must restrict admission of candidates to those who have had at least two years of premedical work in an approved college, including courses in physics, chemistry and biology.

(6) A candidate seeking admission to an approved school, after attendance in a nonapproved school, must receive specific approval from the Authority both as to admission and status after admission.

(7) A candidate admitted to advanced standing must spend at least one year in the school, completing the regular fourth or last-year course of study, if the four-year course is given, or the year next preceding the year of internship, if internship is required for graduation, before the degree is conferred. Before admission to such fourth year, the candidate seeking admission to advanced standing must fulfill all the conditions required of candidates for admission to the fourth year who have taken the uninterrupted course.

(8) The administration of the school must be under the supervision and control of a dean or other administrative officer who is familiar with contemporary medical education, its standards and procedures and who has authority adequate for the proper performance of his duties.

(9) The school must provide adequate preclinical courses in anatomy (including histology and embryology), physiology (including biochemistry and pharmacology) and pathology (including bacteriology and immunology). Average courses for these groups are approximately as follows: anatomy group 15 per cent of the whole medical course; physiology group 15 per cent; pathology group 15 per cent. The whole medical course should cover approximately four thousand (4000) hours.

(10) For the preclinical courses there should be no less than nine full-time teachers of professional rank: for anatomy group, three; physiology group, three; pathology group, three. There must be adequate full-time or part-time assistants, and technicians. This estimate is on the basis of fifty students in each class.

(11) In order that a teacher may be regarded as ade-

quate for a full time professorship (professor, associate professor, assistant professor) he must (1) have had adequate opportunity to become familiar with his subject (2) have had adequate experience as a teacher of his subject, and (3) have attained such a position in his profession that he is recognized by his fellow workers in his specialty as competent

(12) The laboratories for each preclinical subject must be adequate with ample desk room for work, and locker room for supplies and equipment

(13) Each department must have equipment adequate for its needs, for demonstration purposes as well as for routine work with students, for research by members of the faculty, and there must be a sufficient number of rooms for meetings of whole classes for lectures or demonstrations with accessory apparatus for these purposes

(14) There must be an adequate working library for the school, with books of reference and magazine files and tables or desks for work, under the charge of a competent librarian

(15) There must be adequate clinical material available for teaching purposes, for all branches of medicine with especial emphasis on medicine, surgery and obstetrics

(16) The records of the school must be adequate to show the actual condition of the school, and the status of each student, including his premedical record

(17) The financial statement of the school must be so presented as to show whether the school is or is not actually conducted in accordance with its charter as a noncommercial institution

#### QUALIFICATIONS AND EXAMINATION OF APPLICANTS FOR REGISTRATION AS QUALIFIED PHYSICIANS

Amendment of Section 2, Chapter 112, of the General Laws (Acts of 1939, Chapter 451, Section 37), approved August 10, 1939

**Section 2** Applications for registration as qualified physicians, signed and sworn to by the applicants shall be made upon blanks furnished by the board of registration in medicine, herein and in section three to twenty-three, inclusive, called the board. Each applicant who shall furnish the board with satisfactory proof that he is twenty-one or over and of good moral character, that he possesses the educational qualifications required for graduation from a public high school, that he has completed two years of premedical collegiate work, including physics, chemistry and biology, in a college or university approved by a body consisting of the secretary of the board, the commissioner of education and the commissioner of public health, in this section referred to as the approving authority, that he has attended courses of instruction for four years of not less than thirty-two school weeks in each year, or courses which in the opinion of the board are equivalent thereto in one or more legally chartered medical schools, and that he has received the degree of doctor of medicine, or its equivalent, from a legally chartered medical school having the power to confer degrees in medicine and approved by the approving authority, shall, upon payment of twenty-five dollars, be examined, and if found qualified by the board be registered as a qualified physician and entitled to a certificate in testimony thereof, signed by the chairman and secretary. An applicant ag-

grieved by the refusal of the approving authority to approve a medical school under this section shall be entitled to have the reasonableness of such refusal reviewed by a justice of the superior court, whose decision shall be final. An applicant failing to pass an examination satisfactory to the board shall be entitled within one year thereafter to a reexamination at a meeting of the board called for the examination of applicants, upon payment of a further fee of three dollars, but two such reexaminations shall exhaust his privilege under his original application. The board, after due notice, and hearing, may revoke any certificate issued by it to, and cancel the registration of, any physician convicted of a felony, and may, at any time after the expiration of one year thereafter, reissue any certificate so revoked, and register anew any physician whose registration was so canceled. The board, after due notice and hearing, may suspend, for a period not exceeding one year, any certificate issued by it to and cancel the registration of, any physician who has been shown at such hearing to have been guilty of gross and confirmed use of alcohol in any of its forms while engaged in the practice of his profession, or of the use of narcotic drugs in any way other than for therapeutic purposes, or of abuse of the authority granted in section two hundred and nine A of chapter ninety-four or of publishing or causing to be published, or of distributing or causing to be distributed, any literature contrary to section twenty-nine of chapter two hundred and seventy-two or of acting as principal or assistant in the carrying on of the practice of medicine by an unregistered person or by any person convicted of the illegal practice of medicine or by any physician whose registration has been canceled, and whose certificate has been revoked or suspended, by the board, or of aiding and abetting in any attempt to secure registration, either for himself or for another, by fraud, or in connection with his practice, of defrauding or attempting to defraud any person. Except as otherwise provided herein, the board may, at any time, reissue any certificate so revoked and register anew any physician whose registration was canceled.

The approving authority shall, upon the request of any college, university or medical school in this Commonwealth, inspect said college, university or medical school and notify its trustees or other governing body in writing if said college, university or medical school is approved by the approving authority for the purposes of this section, or if not, what steps said college, university or medical school must take in order to gain the approval of the approving authority.

Any college, university or medical school desiring to be approved for the purpose of this section may file with the approving authority a written request for the approval of such college, university or medical school, and thereupon a public hearing shall be seasonably granted by the approving authority and a written decision made by it within twenty days after the termination of such hearing and the applicant for such approval shall be notified of such decision. A written decision of the approving authority refusing to approve any college, university or medical school shall not become effective until thirty days after written notice of such decision is given to the college, university or medical school seeking such approval. Every such college, university or medical school aggrieved by such refusal shall have the right to file a

petition in the superior court for Suffolk County to revise or reverse the decision of the approving authority. Notice of the entry of such petition shall be given to the secretary of the board of registration in medicine and all proceedings connected therewith shall be according to rules regulating the trial of civil causes without juries. The court shall hear the case and finally determine whether or not such approval shall be granted or revised.

Upon the filing of such a petition within the aforesaid period of thirty days, then the said decision of the approving authority shall not become effective until a final decree affirming said decision is entered upon the aforesaid petition.

The board shall examine an applicant who is an alien only if he presents to it a certificate from the court in which he shall have filed his declaration of intention to become a citizen of the United States, or from the Immigration and Naturalization Service of the United States, showing that he has declared his intention to become such a citizen, or a copy of such declaration of intention, certified by the clerk of such court. In case the applicant is subsequently registered, unless he shall present to the board, within five years following the filing of the certificate or certified copy hereinbefore referred to, his completed naturalization papers showing that he is a citizen of the United States his certificate of registration shall be revoked and his registration canceled. The foregoing provisions of this paragraph shall not apply to limited registration under section nine or section nine A or to any alien physician of distinguished merit and ability, duly licensed to practice his profession in any foreign country wherein the requirements for the issuance of such a license are not substantially lower than those of this commonwealth, while he is temporarily teaching in this commonwealth in a medical school approved by the approving authority.

Section 3, Chapter 112, of the General Laws (Acts of 1936, Chapter 247):

*Section 3.* The provisions of said section two of said chapter one hundred and twelve as existing immediately prior to January first, nineteen hundred and forty-one, shall continue to govern as to the eligibility of any applicant for registration as a qualified physician who shall have matriculated prior to said date in any legally chartered medical school having power to confer degrees in medicine, but subject, however, to the provisions of section two of chapter one hundred and seventy-one of the acts of nineteen hundred and thirty-three.

## SECTION OF OBSTETRICS AND GYNECOLOGY\*

### FATAL NEPHRITIS IN PREGNANCY

A thirty-seven-year-old para III had had no prenatal care. When she was approximately twenty-four weeks pregnant, she called a physician because of bleeding. He referred her immediately to the hospital. For two weeks, the patient had

had considerable swelling of the face, abdomen and legs, with blurred vision and epigastric pain.

On examination, the blood pressure was 158 systolic, 100 diastolic. Four hours after entry, the patient delivered herself spontaneously of twins. The kidneys subsequently shut down, and the patient succumbed to uremia a week after admission. Autopsy showed chronic nephritis as the cause of death.

*Comment.* This death cannot be attributed to poor obstetrics; ignorance or indifference on the part of the patient was the real cause of death. Had this patient been seen early in her pregnancy, the diagnosis of chronic nephritis would undoubtedly have been made, and if the condition had not appeared serious enough to warrant abortion, she would have been under constant medical control.

It is commonly believed that any patient with nephritis who is pregnant and shows serious suppression of kidney function as early as five months must have considerable chronic kidney damage. The only way to prevent such deaths is to impress on the laity the value of early prenatal care. If this advice is not generally promulgated and if clinics are not established for all pregnant women, such a disaster as this must recur. Even though the necessity of prenatal care is well recognized and clinics are made available for everyone, no law compels the pregnant woman to accept these advantages, and a few such disasters are bound to occur.

### DEATHS

**BARTLETT**—WALTER O. BARTLETT, M.D., of Boston, died November 5. He was in his sixty-third year.

Born in Natick, Dr. Bartlett received his degree from Harvard Medical School in 1902. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

His mother, a brother and a sister survive him.

**EDGAR**—WILLIAM L. EDGAR, M.D., of Athol, died October 11. He was in his seventieth year.

Dr. Edgar received his degree from the Hahnemann Medical College of Philadelphia. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

**LEACH**—ALBERT C. LEACH, M.D., of Orange, died November 9. He was in his seventy-first year.

Born in Portsmouth, New Hampshire, Dr. Leach received his degree from Dartmouth Medical School in 1894. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

He is survived by his widow, two daughters and two sons.

**LORD**—FREDERICK T. LORD, M.D., of Boston, died November 4. He was in his sixty-seventh year.

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, Secretary, 330 Dartmouth Street, Boston.

Born in Bangor, Maine, Dr Lord received his degree from Harvard Medical School in 1900. After internship at the Massachusetts General Hospital, he was appointed to the staff in 1903 and was a member of its board of consultation at the time of his death. He was made a member of the faculty of the Harvard Medical School in 1905 and served for many years, being appointed professor of clinical medicine in 1930 and professor emeritus in 1935. He was a former vice president of the National Tuberculosis Association, and at the time of his death was president of the Massachusetts Tuberculosis League. He was a fellow of the Massachusetts Medical Society and the American Medical Association and a member of the Association of American Physicians, the American Society for Clinical Investigation and the American Clinical and Climatological Association.

His daughter and two grandchildren survive him.

## CORRESPONDENCE

### URINARY FINDINGS BEFORE AND AFTER A MARATHON RACE

To the Editor: The accompanying chart of urinalyses, prepared by William T. Wright, chief technician of the

renal excretory reaction to the long sustained effort involved in a twenty-six mile race. Various other observers have made similar reports following athletic contests, and this chart is presented simply as additional corroborative evidence of normal kidney response to strenuous exercise.

Urine specimens were obtained both before and after the 1941 Boston marathon race from twenty participants—a fairly good number, considering the size of the starting list, the fact that some starters drop out, the physical condition of the runners at the finish, and the general confusion prevailing.

Several of the determinations were of little or no significance. Following the race, the color tended to be stronger, and the majority of specimens, which had previously been clear, were cloudy or hazy. All but three were acid before and after the race, and of the three that were very faintly alkaline before the race, two were acid afterward. The specimen from one contestant (No. 11) gave a faintly positive test with phenylhydrazine before the race, and that of another (No. 1) afterward. One (No. 8) showed a trace of acetone before the race, and two others (Nos. 16 and 20) showed 4 mg per 100 cc. and a trace, respectively, afterward.

The chart is self-explanatory. The interesting features,

#### Significant Urinary Findings before and after the 1941 Boston Marathon Race

CON- TEST NO.	ORDER OF ANALY- SIS	SPECIFIC GRAVITY		ALBUMIN		BENEDICT'S TEST		FERMENTABLE SUGARS		SEDIMENT	
		BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER
				mg	%			gm / 100 cc	gm / 100 cc		
1	2	1.012	1.030	0	0.10	0	H gr cl	0.01	0.01	Normal	72 gran and 1 y l c s s per 1 p f
2	8	1.024	1.024	0	0.07	F gr cl	H gr cl	0.05	0.05	2 hyal casts per slide	12 f gran and 1 y l c s s per 1 p f
3	11	1.026	1.030	0	0.01	F gr cl	H gr cl	0.08	0.01	1 hyal and 1 f gran cast per slide	116 gran and 1 y l c s s per 1 p f
4	23	1.023	1.025	0	0.08	F hazy	H gr cl	0.04	0.0*	1 hyal cast per slide	30 f gran casts per 1 p f
5	26	1.023	1.010	0	0.02	0	H gr cl	0.03	0.0*	Rare red blood cell	8 hyal casts per 1 p f
6	29	1.022	1.016	0	0.10	0	Gr cl	0.03	0.03	1 hyal cast per slide	35 brown sh gran c s s per 1 p f
7	40	1.007	1.015	0	0.01	0	Gr cl	0.00	0.00	Many spermatozoa	1 f gran cast per slide me spermatozoa
8	41	1.019	1.010	0	0.01	0	0	0.00	0.01	Very rare red blood cell	54 f gran and hyal casts per 1 p f
9	44	1.003	1.027	0	0.15	0	H gr cl	0.00	0.07	Normal	30 f gran and hyal c s s per 1 p f
10	49	1.022	1.032	0	0.25	F hazy	Yell gr cl	0.04	0.03	1 hyal cast per slide	450 gran and 1 y l c s s per 1 p f
11	52	1.028	1.028	0	0.01	H gr cl	Yell gr cl	0.06	0.02	Normal	12 brown sh gran c s s per slide
12	54	1.025	1.025	0	0.05	0	F l c	0.05	0.04	Normal	20 gran casts per 1 p f
13	59	1.027	1.032	0	0.32	F hazy	H gr cl	0.03	0.02	Normal	Normal
14	60	1.014	1.033	0	0.40	0	H gr cl	0.06	0.00	1 hyal cast per slide rare red blood cell	72 f gran and 1 y l c s s per 1 p f
15	65	1.012	1.016	0	0.04	0	H gr cl	0.08	0.01	4 hyal c s s per slide rare spermatozoa	25 cellular (?) casts per 1 p f
16	0+	1.030	1.030	0	0.04	F hazy	H gr cl	0.10	0.01	Rare red blood cell	10 hyal casts per slide
17	0+	1.000	1.014	0	0.03	0	F gr cl	0.00	0.03	Normal	35 f gran and hyal c s s per 1 p f
18	0+	1.010	1.016	0	0.04	0	H gr cl	0.00	0.02	Normal	234 hyal casts per 1 p f
19	0+	1.008	1.016	0	0.03	0	H gr cl	0.00	0.01	Normal	3 hyal and 1 f gran cast per slide
20	0+	1.015	1.018	0.04	0.01	0	F hazy	0.08	0.06	Very rare spermatozoon	306 gran casts per 1 p f

Alters at onset of (Benedict's test) — faint — green — cloudy — heavy — yellow — hyaline — (sediment) — finely gran.

— granular — low power field

\*Ran only 11 miles

John Hancock Mutual Life Insurance Company medical laboratory, may be of some clinical interest in depicting

of course, are the occurrence, following the race, of an incredible number of casts in most of the urines, as shown

by low-power microscopic field, and the consistent finding of albumin in varying quantities (0.01 to 0.04 per cent of albumin is equivalent to a very faint trace or faint trace as shown by the heat test or the nitric acid ring test). It should be noted that no red blood cells were found. Interesting, too, are the reactions to Benedict's test after the race, some of which might be interpreted as showing considerable sugar, although the actual quantity of fermentable sugar was extremely small in all cases (the fermentable-sugar percentage was determined by comparison of picramic acid colorimetric readings both before and after fermentation of the urine and not by the ordinary saccharometer, which is of questionable accuracy). Only one contestant (No. 2) furnished a subsequent specimen, which was procured four weeks later during a rest period while in training for a twenty-mile race; this urine was entirely normal, both chemically and microscopically.

ROLAND A. BEHRMAN, M.D.  
Associate Medical Director

John Hancock Mutual Life Insurance Company  
Boston

## MISCELLANY

### RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR SEPTEMBER, 1941

DISEASES	SEPTEMBER 1941	SEPTEMBER 1940	FIVE-YEAR AVERAGE*
Anterior poliomyelitis	67	14	37
Chicken pox	106	105	83
Diphtheria	10	7	13
Dog bite	1197	955	895
Dysentery, bacillary	110	17	22
German measles	28	18	22
Gonorrhea	403	391	484
Measles	168	211	114
Meningitis, meningococcal	8	—	3
Meningitis, other forms	2	—	—
Mumps	233	125	122
Paratyphoid fever	2	3	10
Pneumonia, lobar	107	135	119
Scarlet fever	246	128	144
Syphilis	361	403	429
Tuberculosis, pulmonary	248	251	235
Tuberculosis, other forms	26	32	26
Typhoid fever	7	5	12
Undulant fever	8	9	4
Whooping cough	546	474	471

\*Based on figures for preceding five years

### GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from: Attleboro, 2; Barnstable, 1; Billerica, 1; Boston, 9; Brockton, 2; Cambridge, 3; Danvers, 1; Fall River, 2; Falmouth, 2; Fitchburg, 1; Hanson, 1; Haverhill, 1; Lakeville, 1; Lynn, 1; Manchester, 1; Medford, 1; Melrose, 2; Merrimac, 1; Middleborough, 1; Natick, 2; New Bedford, 3; Newton, 2; North Attleborough, 2; North Brookfield, 1; Salem, 1; Sharon, 1; Somerville, 2; Southwick, 1; Spencer, 1; Springfield, 2; Sterling, 1; Stoneham, 1; Swansea, 2; Taunton, 1; Wareham, 1; Watertown, 1; Westwood, 1; Wilbraham, 1; Williamstown, 1; Worcester, 5; total, 67.

Diphtheria was reported from: Fall River, 9; Somerville, 1; total, 10.

Dysentery, bacillary, was reported from: Boston, 2; Danvers, 6; Dunstable, 91; Fairhaven, 1; Lowell, 1; Northampton, 1; Watertown, 1; Winchester, 1; Worcester, 6; total, 110.

Infectious encephalitis was reported from: Fall River, 1; Worcester, 1; total, 2.

Meningitis, meningococcal, was reported from: Chico-

pee, 1; Easthampton, 1; Fort Devens, 1; Framingham, 1; Ipswich, 1; Manchester, 1; Quincy, 2; total, 8.

Meningitis, other forms, was reported from: Cambridge, 1; Lowell, 1; total, 2.

Paratyphoid fever was reported from: Boston, 1; Brookline, 1; total, 2.

Pellagra was reported from: Boston, 2; Fall River, 1; total, 3.

Rocky Mountain spotted fever was reported from: Quincy, 1; total, 1.

Septic sore throat was reported from: Fall River, 1; Boston, 1; total, 2.

Tetanus was reported from: Brockton, 1; total, 1.

Trachoma was reported from: Worcester, 1; total, 1.

Trichinosis was reported from: Boston, 4; Fall River, 1; Medford, 2; Middleborough, 1; total, 8.

Typhoid fever was reported from: Chicopee, 2; Fall River, 1; Marblehead, 1; Scituate, 1; Winthrop, 1; Woburn, 1; total, 7.

Undulant fever was reported from: Carver, 1; Leominster, 1; Newburyport, 1; Northampton, 1; Pittsfield, 1; Somerville, 1; Templeton, 1; Webster, 1; total, 8.

Anterior poliomyelitis has increased slowly this season but has not reached epidemic proportions.

Meningococcal meningitis, pulmonary tuberculosis, scarlet fever, undulant fever and whooping cough were above the five-year averages.

Chicken pox, German measles, measles, mumps, scarlet fever and whooping cough, although slightly above the five-year averages, have shown the usual seasonal declines.

Dog bite not only has shown the usual seasonal increase but has reached record high figures for the month.

Bacillary dysentery has shown a steady increase this summer and has reached record high proportions for September.

Diphtheria, gonorrhea, lobar pneumonia, paratyphoid fever, typhoid fever and syphilis were below the five-year averages.

## NOTES

Award of the Louis E. Kirstein Fellowship to Dr. Sidney Cohen, A.B. '33, M.D. '37, assistant in medicine and in bacteriology, was among the grants of \$5925 at the Harvard Medical School for the current academic year recently announced by Harvard University. This fellowship, to promote "scientific medical education," was established through a gift made to Harvard University by eighty-nine friends of Mr. Kirstein in honor of his seventieth birthday and in recognition "of their affection for him as a man and their admiration of him as a humanitarian." Kenneth T. Bird, 4M, of Watertown, was awarded the James C. Melvin Scholarship. National Scholarship renewals were awarded to James S. Clarke, 2M, of La Grange, Illinois; Martin E. Flipse, 2M, of Douglaston, Long Island, New York; Winsor C. Schmidt, 2M, of Rye, New York; Louis E. Ward, 3M, of Mt. Vernon, Illinois; Allan L. Friedlich, Jr., 3M, of New York City; Glen R. Leymaster, 4M, of Aurora, Nebraska; Clarke T. Case, 4M, of Pynmana, Burma; and Laurence G. Wesson, Jr., 4M, of Boston.

Dr. Bennett F. Avery, dean of Boston University School of Medicine, recently announced that the Samuel Gold Award, presented annually to the school's outstanding first-year student by Phi Lambda Kappa fraternity, has been given to Sarkis A. Sarkisian, of Bridgewater.

## NOTICES

## ANNOUNCEMENTS

Dr. RALPH H. HOPKINS announces the removal of his office from the Hotel Westminster, Boston, to 31 Bay State Road

Dr. DAVID W. WELLS announces the removal of his office from the Hotel Westminster, Boston, to 31 Bay State Road

## BOSTON MEDICAL HISTORY CLUB

There will be a meeting of the Boston Medical History Club at the Boston Medical Library, 8 Fenway, on Wednesday, November 19, at 8:15 p.m. Dr. Arturo Castiglioni will speak on Giovanni Battista Morgagni in relation to the evolution of medical thought in the eighteenth century

All interested persons are cordially invited to attend

ROBERT DAWSON EVANS  
MEMORIAL LECTURE

Dr. ALVAH H. GORDON, professor of medicine emeritus at McGill University Faculty of Medicine Montreal, will give the first in the series of Robert Dawson Evans Memorial Lectures on Friday, November 21 at 8:15 p.m. in the Evans Auditorium, 78 East Concord Street, Boston. His subject will be Bone Changes in Certain Medical Diseases.

Physicians and medical students are cordially invited to attend

## BOSTON SOCIETY OF BIOLOGISTS

A meeting of the Boston Society of Biologists will be held at the Harvard Biological Laboratories, Divinity Avenue, Cambridge, on Wednesday, November 19 at 8 p.m.

## PROGRAM

Chronic Gonadotropin and Luteal Secretion in Primates Dr. Frederick L. Hisaw

On Seasonal Changes in the Testes of Deer and Their Relationship to the Growth of Antlers Dr. George B. Wislocki

Biochemical Aspects of Antler Growth Dr. Joseph C. Aub, Miss Regina McLean and Miss Dorothy M. Tibbets

## WALTHAM MEDICAL MEETING

The regular clinicopathological staff conference of the Metropolitan State Hospital will be held at the hospital on Wednesday, November 26, at 8 p.m. Two cases of diabetes will be presented by Drs. Clementine McKeon, Richard C. Wadsworth and Elvin V. Semrad and will be discussed by Dr. Alexander Marble.

All interested physicians are cordially invited to attend

MASSACHUSETTS SOCIETY  
OF EXAMINING PHYSICIANS

The Massachusetts Society of Examining Physicians will have its fall meeting and dinner on Wednesday evening, December 3, at 6:30 p.m., at the Copley Plaza, Boston.

Dr. J. Grafton Love, of the Neuro Surgical Department,

Mayo Clinic, Rochester, Minnesota, will present a paper entitled, "Protruded Intervertebral Disks: A common cause of disabling backache and sciatic pain," which will be illustrated with lantern slides and motion pictures. Dr. W. Jason Mixer, chief of the Department of Neuro-Surgery, Massachusetts General Hospital, and Dr. Gilbert E. Haggart, chief of the Section of Orthopedic Surgery, Lahey Clinic, will discuss the paper.

NEW ENGLAND HEART  
ASSOCIATION

The next meeting of the New England Heart Association will be held on Monday, November 24, at 8:15 p.m. at the Massachusetts General Hospital.

## PROGRAM

Pulmonary Embolism and the Electrocardiogram Drs. Donald Murnaghan, Sylvester McGinn and Paul D. White.

Follow-Up Study of Cases of Chronic Constrictive Pericarditis Drs. Marlow B. Harrison and Paul D. White.

Phonocardiography Dr. Howard B. Sprague and Mr. Maurice B. Rappaport.

Follow-Up Study of Uncomplicated Systolic Murmurs at the Cardiac Apex or Aortic Valve Area Drs. Lyle Baker, Howard B. Sprague and Paul D. White.

Clinicopathological Study of Marked Coronary Disease Drs. Reno R. Porter and Edward F. Bland.

Interested physicians and medical students are cordially invited to attend.

NEW ENGLAND SOCIETY  
OF PHYSICAL MEDICINE

A meeting of the New England Society of Physical Medicine will be held on Wednesday, November 19, at 8 p.m., at the Danvers State Hospital, Hathorne, Massachusetts.

## PROGRAM

Introductory Remarks Dr. Clarence Alden Bonner, superintendent, Danvers State Hospital.

Neuropsychiatric Clinic, with a Discussion of Indications for Physical Medicine. Presentation of cases of multiple sclerosis, Raynaud's disease, parkinsonism, manic-depressive psychosis and schizophrenia. Dr. Leo Maletz, clinical director, Danvers State Hospital.

All members of the medical profession are cordially invited to attend.

AWARD BY THE AMERICAN  
UROLOGICAL ASSOCIATION

The American Urological Association offers an annual award, not to exceed \$500, for an essay (or essays) on the result of some specific chemical or laboratory research in urology. The amount of the award is based on the merits of the work presented, and if the Committee on Scientific Research considers none of the offerings worthy, no award will be made. Only residents in urology in recognized hospitals and physicians who have practiced urology for not more than five years may compete.

Essays should be in the hands of the secretary, Dr. Clyde L. Deming, 789 Howard Avenue, New Haven, Connecticut on or before April 1, 1942.

## UNITED STATES CIVIL SERVICE EXAMINATIONS

Health-Education Consultants, \$2600 to \$3800 a Year

To assist state, county and local health officers in dealing with problems incident to the rapid growth in industrial and governmental production and the consequent unusual concentration of population and increasing health problems, the United States Public Health Service is planning to appoint health-education consultants to various defense areas. The positions, paying \$2600 to \$3800 a year, will be filled through open competitive examinations, and the United States Civil Service Commission has just issued the examination announcement. A written test will not be given, but applicants will be rated on their qualifications as shown in their applications and corroborative evidence.

Appointees will work with local health officers and their staffs, advising them regarding methods of health education, such as individual instruction through interview, group instruction through discussions, talks, lectures and other educational technics. To qualify for the positions, applicants must have completed a four-year college course, including or supplemented by special study—or for the assistant grade, experience—in public health. In addition, they must have had experience in public-health education work co-ordinating the activities of all organized health groups in a community for the purpose of promoting a public-health program. This experience must have been in a federal, state or official local public-health department or in a voluntary agency, such as the American Red Cross or the National Tuberculosis Association.

Applications must be filed with the Civil Service Commission in Washington, D. C., not later than December 11, 1941. The examination announcement giving detailed requirements can be consulted or obtained at any first-class or second-class post office or at the central office in Washington.

## EXAMINATIONS FOR APPOINTMENTS IN THE MEDICAL CORPS OF THE UNITED STATES NAVY

Examinations for appointment as assistant surgeon (lieutenant, junior grade), United States Navy Medical Corps, will be held at all the large naval hospitals and the Naval Medical Center, Washington, D. C., on January 5 to 9, 1942, inclusive.

Applicants for appointment as assistant surgeon must be citizens of the United States, more than twenty-one but less than thirty-two years of age at the time of acceptance of appointment, and graduates of Class A medical schools who have completed at least one year of intern training in a hospital approved by the Council on Medical Education and Hospitals of the American Medical Association.

Examinations for appointment as acting assistant surgeon for intern training in naval hospitals accredited for intern training by the Council on Medical Education and Hospitals of the American Medical Association will also be held on January 5 to 9, 1942, inclusive. Applicants for appointment as acting assistant surgeon for intern training must be citizens of the United States, more than twenty-one but less than thirty-two years of age, and members of the junior or senior classes in Class A medical schools. After twelve months of intern training, acting assistant surgeons may apply for appointment as assistant surgeons in the United States Navy.

A circular of information regarding these examinations, physical requirements, rates of pay and promotion and retirement data may be obtained from the Bureau of Medicine and Surgery, Navy Department, Washington, D. C., on request. Applications for authorization to take the examination must be received at the Bureau of Medicine and Surgery three weeks before the examination.

Medical officers of the United States Navy are encouraged to develop a specialty, and are assigned, if their interest in the specialty warrants such action, to postgraduate instruction in the large naval hospitals, the Naval Medical Center, Washington, D. C., and civilian medical centers. Some of the specialties in which medical officers may seek qualifications are: surgery, medicine, ophthalmology, otolaryngology, roentgenology, laboratory, pathology, public health, psychiatry, deep-sea diving, aviation medicine (flight surgery), gas warfare, tropical medicine, medical research and so forth.

## SOCIETY MEETINGS AND CONFERENCES

### CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, NOVEMBER 16

#### MONDAY, NOVEMBER 17

12 15-1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

#### TUESDAY, NOVEMBER 18

\*9 00-10 00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H Pratt Diagnostic Hospital.

12.00 m. Treatment of Epilepsy. Dr. H. Houston Merritt. South End Medical Club. Headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston.

12 15-1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital amphitheater.

#### WEDNESDAY, NOVEMBER 19

\*9 00-10 00 a.m. Refractory Blood Diseases. Dr. C. W. Heath. Joseph H. Pratt Diagnostic Hospital.

\*12 00 m. Clinicopathological conference. Children's Hospital

4 30 p.m. New England Oto-Laryngological Society. Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston.

8 00 p.m. Boston Society of Biologists. Harvard Biological Laboratories, Divinity Avenue, Cambridge.

\*8 15 p.m. Giovanni Battista Morgagni. Dr. Arturo Castiglioni. Boston Medical History Club. Boston Medical Library, 8 Fenway

#### FRIDAY, NOVEMBER 21

\*9 00-10 00 a.m. Anemia and Hiatus Hernia. Dr. William P. Murphy. Joseph H. Pratt Diagnostic Hospital.

\*8 15 p.m. Bone Changes and Certain Medical Diseases. Dr. Alvah H. Gordon. Evans Auditorium, Massachusetts Memorial Hospitals

#### SATURDAY, NOVEMBER 22

\*9.00-10.00 a.m. Blood Clinic. Dr. H. G. Brugsch. Joseph H Pratt Diagnostic Hospital.

\*Open to the medical profession.

NOVEMBER 17-19, 21-22, 27 and 30. Thomas William Salmon Memorial Lectures. Page 636, issue of October 16.

NOVEMBER 19. New England Society of Physical Medicine. Page 803

NOVEMBER 24. New England Heart Association. Page 803

NOVEMBER 26. Waltham Medical Meeting. Page 803.

DECEMBER 3. Massachusetts Society of Examining Physicians. Page 603.

DECEMBER 11. Pentucket Association of Physicians. Page 473, issue of September 18.

JANUARY 3. American Board of Obstetrics and Gynecology. Page 473, issue of September 18.

JANUARY 10-11. Forum on Allergy. Page 392, issue of September 4

FEBRUARY 19-21. American Orthopsychiatric Association. Page 708, issue of October 30.

APRIL 6-10. American Congress on Obstetrics and Gynecology. Page 600, issue of October 9.

APRIL 8-11. American Academy of Physical Medicine. Hotel Statler, Boston.

APRIL 20-24. American College of Physicians. Page 996, issue of June 5

## DISTRICT MEDICAL SOCIETIES

### BERKSHIRE

APRIL 30.

(Continued on page x)



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## THE CONSERVATIVE TREATMENT OF OCCLUSIVE ARTERIAL DISEASE\*

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NEW YORK CITY

DURING the last ten years, great advances have been made in the conservative treatment of occlusive arterial disease. Major amputation in the course of the routine care of thromboangiitis obliterans has, as a result of conscientious efforts on the part of many workers throughout the country, become a rather rare occurrence. In 100 consecutive cases treated by the Vascular Clinic of the New York Post-Graduate Medical School and Hospital, major amputations were performed in only 3 cases, and figures similar to these have emanated from several sources. This is in contrast to major amputations in 50 to 70 per cent of cases prior to the use of the newer methods. We have been engaged in attempting to determine how much could be accomplished in the way of saving extremities by intensive conservative therapy. It is probable that some of these patients might have been somewhat better off financially and that their periods of disability might have been shortened by amputation earlier in the course of treatment. It is my belief, however, after studying these cases, that this figure would probably not be higher than 10 per cent. Moreover, amputation is considered the easiest course; it requires no courage, and very little can be learned from it. Conclusions that have resulted from conscientious, painstaking care of the difficult cases have often been applied with great success in the care of the less advanced lesions.

The problems associated with arteriosclerosis obliterans are more difficult. As has been pointed out previously,<sup>1</sup> this is one of the greatest economic, social and medical questions confronting the American people. There are roughly 25,000,000 people over the age of fifty in the United States today. This number is rapidly increasing, owing

to the age shift in the population. Of these persons, 60 per cent, or 15,000,000, will die of cardiovascular disease, for the most part associated with arteriosclerosis obliterans affecting the vessels of the heart, brain, kidney and other parts of the body. By contrast, only 9 per cent will die of cancer. Yet the endowments for cancer and the facilities for research in that very dramatic field have been far in excess of those available for the study of the heart and blood vessels. In spite of this neglect, material that has inconspicuously been accumulated has resulted in a better understanding of the physiologic pathology involved and has laid a sound groundwork for a more intelligent approach to the problem of treatment. The marked diminution in the amputation rate and the greater percentage of restoration in walking ability in cases of intermittent claudication have been somewhat in excess of anticipation. To date, however, this has not resulted in such satisfactory results as those obtained in the treatment of thromboangiitis obliterans.

Although there are more than fifty recognized vascular diseases and syndromes, each disease and, in fact, each patient should be studied on the basis of the exact status of the circulation of the patient. Certain forms of therapy are especially helpful in the treatment of the major occlusive arterial diseases, thromboangiitis obliterans and arteriosclerosis obliterans. I propose to discuss the conservative aspect of these forms of treatment very briefly.

### Rest

One of the most important factors in the treatment of any patient with ulceration or gangrene is rest. This should be used intelligently and on the basis of sound physiology. If the extremity is elevated, it easily becomes ischemic, and a tendency toward gangrene results. If it is kept dependent, the blood flow toward the heart be-

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comes more difficult, and congestion, with a relative ischemia, may arise. Reid<sup>2</sup> has shown that the correct level is the point at which the tip of the extremity is from 7 to 15 cm. (3 to 6 inches), below the level of the heart. At this level, gravity assists the flow of arterial blood into the limb, and the blood is not retarded in its return by too greatly increased venous back pressure. Rest should be continued until the lesion is healed, except in the specific vascular exercises enumerated below.

### *Active Vascular Exercises*

Buerger<sup>3</sup> has described vascular exercises that, since they are in wide use today, do not necessitate an elaborate description of the original suggestions. I should like to propose, however, the following modification, which applies to these exercises and is on a more sound physiologic basis than that generally applied. The physician should first elevate the patient's extremity until pallor develops. The length of time necessary for this to occur should be noted. He should then lower the extremity until rubor develops and, again, should measure the time necessary for this change. These times should be given to the patient as indicating the exact periods for elevation and dependency, rather than arbitrary units of time. From time to time in the course of treatment, these reactions should be rechecked, and the indicated changes in instructions to the patient should be given.

Allen<sup>4</sup> has suggested a modification of Buerger's exercises in which the foot is extended downward and raised by flexion of the ankle joint; the toes are turned inward and then outward, and are then separated and closed. This is helpful, if it is not too painful.

### *Care of the Extremities*

Meticulous care of the skin and nails of extremities that are suffering from impaired circulation is of vital necessity. Hands or feet that have not yet developed ulceration or gangrene should be bathed daily, and the skin and nails kept soft by the subsequent application of lanolin, olive oil or other substances having a similar effect. Nails and calluses must be pared with great care, since a very large percentage of ulcers are precipitated as a result of minute injuries that would normally heal promptly. The use of strong dekeratinizers, such as salicylic acid (in high percentage), is not to be recommended; if they are used for stubborn calluses, the situation must be kept under careful observation.

Frequent examinations should be made for evidence of epidermophytosis, since the cracks produced by this condition are frequent portals of entry for very serious secondary bacterial invaders. In my experience, soaks for potassium permanganate in dilutions of 1:7000 to 1:10,000 for thirty minutes every two or three days are usually a satisfactory method of controlling this fungus. It is advisable, however, to continue these soaks at weekly intervals long after the fungus has apparently disappeared. Gentian violet in a 5 per cent aqueous solution may be used, but the stronger antiseptics and fungicides are distinctly contraindicated, since the condition of the tissues is frequently such that more harm than good results.

When ulceration occurs, the problem immediately becomes more serious and emergent. This fact is too often not recognized or acted on by the physician. There is a dictum in our clinic: It is far better surgery to take meticulous care of a minute lesion than it is to perform a major amputation in the amphitheater. The cutting away of the involved area before the available circulation has been adequately improved usually results in a larger ulceration, with an unfavorable result. Efforts, such as those subsequently outlined in this paper, should be made to improve the blood supply, since that is the primary problem. Soaks should be used. All strong antiseptics, such as iodine and the mercurials, should be avoided: they frequently do more harm to the delicate new endothelial buds and new cells than to the infecting organisms. Gradually, by careful daily dissection, sloughs and other debris should be removed, thus allowing the endothelial, epithelial and connective-tissue cells to extend in from the edges. It is essential to make certain that purulent material is not accumulating under the scabs, which often appear healthy and innocuous. Lifting of the edges frequently reveals pus that is eroding and undermining the tissues covered by and surrounding the scab. It is imperative to maintain adequate drainage by removing or cutting windows in the scab; this should be followed immediately by a saline soak.

If the situation results in gangrene of digits or of an entire hand or foot, careful observation should be routine for evidence of rapid extension of infection, such as lymphangitis or a septic syndrome. When this occurs, amputation may be necessary. When, however, the gangrene is slowly extending, time should be allowed for self-amputation whenever possible, since the circulation is usually then adequate for healing at the point of separation. One can help this along by keeping the point of separation clean and by cutting per-

sisting tendons and other fibrous tissue a little at a time. Finally, the digit may be lifted off with little or no discomfort and without a local anesthetic, which is apt to be harmful because of the pressure produced in the tissues. Adrenalin in an anesthetic is especially contraindicated, since it produces vasoconstriction; I have seen cases in which massive gangrene was precipitated by this substance. If the tip of a phalanx protrudes beyond the level of the separation, it will probably be necessary to remove it down to that level on the shaft of the bone. This may be accomplished slowly, in small fragments, by the use of a scalpel—after which healing will tend to take place more satisfactorily. After each dressing, a thirty-minute soak in sterile physiologic saline solution at a temperature of 96°F. helps to ensure drainage and cleanliness, following which the area is dried sterily and kept under dry thermostatically controlled heat, as described elsewhere.

Nerve sections are occasionally used on our service if we are unable to control the pain in any other way, but judging by the results in other clinics as well as those in our own, we are inclined to believe that too frequently the claims of complete relief represent wishful thinking on the part of the surgeon and a disregard of the pain and especially the paresthesias of which the patients complain when permitted to voice their woes. Similar complaints of very annoying paresthesias frequently follow the use of alcohol block of the lumbosacral sympathetic nerves, and surgeons who have never noted such results should spend more time listening to their patients. Nevertheless, one is sometimes obliged to use these measures in an endeavor to bring all possible collateral circulation into play before the gangrene becomes widespread.

A discussion of the surgical technics that are indicated when conservative therapy fails and that require the finest judgment is not within the scope of this paper. It is most important that, when amputation is to be performed, the correct level be determined on the basis of adequate circulation for healing by careful clinical study. In doubtful cases, tests such as oscillometric readings, arteriograms, histaminase-flare reactions, and vasodilatation tests prove useful.

#### *Abstinence from Tobacco*

It hardly seems necessary to elaborate on the need for total and permanent abstinence from tobacco in the care of occlusive arterial disease, since great volumes of experimental evidence confirm the studies of Maddock and Coller,<sup>2</sup> Barker,<sup>6</sup> Wright and Moffat<sup>7</sup> and Lampson.<sup>8</sup> Thrombo-

angiitis obliterans appears to be more specifically aggravated by smoking than arteriosclerosis obliterans,<sup>9-11</sup> but in the latter disease it is essential to realize that, whereas the major vessels may be occluded, the small collateral branches (on which the life of the tissues depends) are subject to spasm. If the blood supply has been reduced by disease to the bare minimum necessary for the life of the tissues, it is disastrous to produce repeated spasm in these small vessels and thus reduce the blood supply to a point incompatible with the life of the tissues. For further investigation on this subject, one may find a review of the points involved in a recent symposium<sup>11</sup> on vascular disease. Clinical experience has shown that if a physician wishes to obtain good results in the treatment of either of these conditions he must impress his patient with the fact that his outlook depends on conformity to the edict, "No smoking, now and forever."

#### *Alcohol*

As a more cheerful and compensatory form of treatment, the use of alcohol may be prescribed. Alcohol has been demonstrated to be a marked vasodilator, and it is also of considerable value as a sedative. We therefore recommend the liberal use of alcohol almost to the point of inebriation during the acute, painful periods of ulceration or gangrene, and its moderate daily use after the lesions have healed and the patient has again become active. It is our experience that patients rarely object to this form of therapy.

#### *Baths*

Various types of baths have been used. We formerly used contrast baths, but there are several reasons why these have been largely abandoned in our clinic. In the first place, the best containers reach only to the knees, and too often the area of blockage is well above that level, so that the changes in the metabolic demands caused by the baths cannot be adequately compensated for by the vessels. Secondly, when already damaged vessels are forced into sudden vasospasm, they may remain closed, thus complicating the picture. Thirdly, many patients complain of the severe pain that occurs during the cold phase. In place of these, we use a modification of the sitz bath, in which the patient sits in a tub containing at least 30 cm. (12 inches) of water at a temperature of 34 to 38°C. (95 to 100°F.) for thirty minutes once a day. This tends to produce vasodilatation of the patient's vessels from the hips down, and is a very satisfactory form of therapy except that it is not recommended when open lesions are present.

## Soaks

In the place of wet dressings, which have largely been abandoned, because unless watched with rare acuity they become cold and chill the small endothelial buds into inactivity, we have used soaks, two or three times daily, for fifteen to thirty minutes. We use a boric acid solution or a physiologic solution of sodium chloride at 36 to 38°C. (96 to 100°F.). Great care should be taken to keep the temperature within these limits. After each soak, the foot is carefully dried and placed under a thermostatically controlled cradle, thus preventing chilling and at the same time allowing for softening of the crusts and adequate drainage.

## Heat

It is probable that the use of local heat has done far more harm than good in the treatment of peripheral vascular disease. I have seen more than 50 cases in which severe ulceration, massive necrosis or gangrene was primarily produced by the extensive use of diathermy or short-wave, infrared or other forms of local heat applied to an area where there was a marked arterial impairment resulting from peripheral vascular disease. When intensive heat is used locally in the presence of marked impairment of the circulation, greatly increased metabolic demands cannot be met, since insufficient blood is available. Furthermore, intensive heat cannot be carried away, so that the tissue rapidly becomes broiled, almost as if it were a piece of meat. I have seen cases in which holes produced by burning, with subsequent necrosis, extended through the flesh of the patients' feet until finally the bones of the feet were exposed. Seven of these patients have lost their legs, and 2 have died. It is therefore vital to use only controlled heat, with the temperature between 31 and 36°C. (88 and 96°F.), depending on the needs of the patient. This can best be accomplished by means of a thermostatically controlled light.

Reflex heat, on the other hand, is of great value.<sup>12</sup> The application of warm pads, short-wave currents, diathermy and so forth to various portions of the body not involved results in a tendency toward reflex vasodilatation of the major vessels and their collaterals distally. It has definite advantages and, so far as we know, is without danger. Wilkins, Doupe and Newman<sup>13</sup> have shown that the increase in blood flow resulting from local heat is not so great as that produced by warming the body.

## Typhoid Vaccine

The intravenous use of typhoid vaccine has been proved to be of great value in the treatment of thromboangiitis obliterans, although we do not recommend its use in cases of arteriosclerosis obliterans. Specially prepared typhoid vaccine should be used. The H antigen prepared by Eli Lilly and Company and recommended by Barker<sup>14</sup> is satisfactory. For some years, we have used typhoid vaccine prepared by the Kirk Biological Laboratories, of Bloomfield, New Jersey. For this purpose, it is diluted to a strength of 100,000,000 organisms per cubic centimeter. It is given intravenously, and the first dose should not exceed 5,000,000 organisms. The object is to produce a fever of 2 or 3°F., *without a chill*. When the repeated dose fails to produce an adequate response, the amount should be increased by 3,000,000 to 5,000,000 organisms. This should be given every three or four days, and a careful temperature chart should be kept.

Administration of this vaccine is continued until the ulceration or gangrene is healed, and for several months thereafter for the purpose of developing adequate collateral vessels. In our experience, the use of typhoid vaccine produces a more rapid response both in release from pain and in healing than the intravenous use of hypertonic saline, citrate or similar solutions.

## Vasodilating Drugs

In general, the use of the vasodilating drugs has been rather disappointing in the treatment of occlusive vascular disease. They may be roughly divided as follows: the nitrites and allied compounds; theobromine, Theocalcine and allied compounds; the choline compounds<sup>15</sup>; and papaverine. Although each of these products has specific indications and values in other fields, in the treatment of these two major vascular diseases, they are of rather doubtful merit. For example, in studies published several years ago,<sup>16</sup> it was shown that reflex heat was much more reliable and effective than papaverine.

## Tissue Extracts

The therapeutic use of various tissue extracts has been studied in our laboratory for ten years. We have employed various extracts prepared from the heart, skeletal muscles, liver and pancreas. Of these, the pancreatic tissue extracts have seemed the most effective in the treatment of intermittent claudication in man. Details of these studies have been reported elsewhere.<sup>17</sup> In brief, however, it is our opinion that the present, relatively pure form

of pancreatic extract (Depropanex) does favorably affect intermittent claudication. Ergometric studies that demonstrate this fact rather clearly have been made.<sup>17</sup> Patients have been enabled to walk longer distances after changing from previous therapy through the single addition of pancreatic tissue extract. More than 200 patients with this syndrome have been studied, slightly over 60 per cent showing a marked improvement and another 15 per cent showing moderate improvement—marked improvement was taken to mean an increase in walking ability whereby a patient who could walk only two or three blocks was finally able to walk ten blocks or more. This, we believe, enables him to carry on most types of occupation in a conservative manner.

This material is injected in doses of 3 cc. intragluteally two or three times a week. It has been established that pancreatic extract is nontoxic when given intravenously, although it is not used by this route in the treatment of intermittent claudication. The exact mechanisms of its action are not very well understood. It is an epinephrine antagonist in rabbits, but has not been shown to have marked vasodilating properties in man. The most popular theory at present is that it acts as a replacement product, supplying a greater concentration in the blood of substances that are essential to correct muscle metabolism but have been reaching the muscle tissue in reduced amounts because of the narrowing of the total vascular bed. Early studies of the effects of pancreatic extracts on the development of atherosclerosis in rabbits fed on cholesterol appeared to indicate that they retarded the deposition of cholesterol in the wall of the aorta. Further studies with additional series of rabbits have, however, failed to confirm this observation.<sup>18</sup> Further fractionation of this substance is now being attempted in the hope of isolating an active principle.

#### *Mechanical Therapy*

Mechanical therapy in various forms has become the vogue rather recently. One of the first of these machines to receive general attention was that known as the pressure-suction boot. Although this principle was used in the treatment of the circulation before 1800, it remained for Landis and Gibbon<sup>19</sup> and Hermann and Reid<sup>20</sup> to perfect mechanized units for this purpose. Since the apparatus has had much widespread publicity and general use, it is not necessary for me to go into the details of the technic. As in most new forms of therapy, the experimental claims were overoptimistic. It was at various times stated to be of value in the treatment of arterio-

sclerosis, thromboangiitis obliterans, Raynaud's syndrome, acute embolism, frostbite and almost every form of circulatory impairment that comes to mind. Actual experience with this apparatus has markedly reduced the indications for its use. At present, it may be said to be of value in the treatment of frostbite, acute embolism (if a well-trained surgical and medical team is not available for the surgical removal of the embolus) and a few selected cases of arteriosclerosis obliterans in which the lesion is small and not infected and the level of blockage is below the level at which the cuff is applied. On the other hand, the following contraindications have been definitely established: the presence of thrombophlebitis—this excludes many cases of thromboangiitis obliterans, since these patients tend to develop thrombophlebitis very easily; the presence of infection in the lesion; and lesions whose level is higher than that at which the cuff can be applied.

#### *Reactive Hyperemia and Intermittent Venous Occlusion*

The use of intermittent venous occlusion has been advocated from several sources. Most of this work is based on the original studies of Lewis and Grant,<sup>21</sup> in which reactive hyperemia, both arterial and venous, was described. We have conscientiously used this apparatus on 23 cases at the New York Post-Graduate Medical School and Hospital. Favorable reports have been published by Collens and Wilensky,<sup>22</sup> de Takats, Hick and Coulter,<sup>23</sup> and Wilson and Ogston.<sup>24</sup> Unfavorable results have been published by Veal and McCord<sup>25</sup> and Allen and McKechnie,<sup>26</sup> and we<sup>27</sup> have also reported unfavorably on the use of this equipment. The reactive hyperemia that undoubtedly occurs is, as pointed out by Roy and Brown<sup>28</sup> and Lewis and Grant,<sup>21</sup> in the final analysis an attempt on the part of the tissues deprived of a proper blood supply to become repossessed of it, and the phenomenon of reactive hyperemia is related in its degree to one factor, namely, the blood-flow debt, which is usually a product of the amount by which flow is reduced and the time over which the reduction has been maintained. We question very strongly the advisability of subjecting these already malnourished tissues to additional periods of deprivation of adequate blood supply to increase the blood flow thereafter, especially when the amount of the blood flow is roughly equal to that developed during the preceding phase of the cycle. We have, therefore, discontinued the use of this form of therapy in our clinic, although—as in all types of treatment—there

are reports of patients who apparently improved while this therapy was being carried on.

### *Vasoscillating Bed*

The third form of mechanical therapy that has been receiving widespread attention is that known as the vasoscillating bed, which was first described by Sanders.<sup>29</sup> By means of this bed, the head and feet of the patient are alternately elevated and lowered, a complete cycle taking from one to three minutes. This is another form of Buerger's exercises, the great difference being that this type may be continued for twenty-four hours a day if necessary, whereas Buerger's exercises can be maintained only for twenty minutes once or twice a day. We do not find it necessary to use this or any other elaborate mechanism in the treatment of thromboangiitis obliterans, but in the treatment of arteriosclerosis obliterans with impending or actual gangrene or ulceration we have found this to be of great value. More than 150 cases have now been studied at our hospital. Although it is difficult in all forms of therapy to evaluate the results satisfactorily, we have become increasingly convinced of its merit. Our experience conforms with the results recently published from the Mayo Clinic<sup>30</sup> and the Vascular Clinic of the Northwestern Medical School.<sup>31</sup> Healing of ulcerations that had previously been extremely obstinate and a general improvement in circulation in many cases have been noted. The progress is relatively slow, and it is frequently necessary to keep the patient on the bed steadily for at least a month. After this time, the patient may be allowed to be up and about during the day, but it is imperative for him to have eight hours' treatment at night on the bed. This is continued over a period of months or even years, and it appears to be of real value in increasing the ability of the collateral vessels to take over the burden of the functions associated with tissue nutrition. We usually employ a thermostatically controlled light as part of the equipment with the bed.

\* \* \*

Of all types of experimental or clinical research, none presents more difficulties than the correct evaluation of therapeutic agents. Many published studies are valueless because the author has neglected to consider other factors that he introduced into the picture simultaneously with the form of treatment that he was attempting to evaluate. Other studies are open to grave question because both known and unknown factors that affect the results were unavoidably present.

A proper estimation of the worth of a new treatment, therefore, rests on its use only in the presence of adequate controls and freedom from extraneous factors that may be influencing the clinical course of the patient. For example, forms of therapy have been reported as being of great value in the treatment of peripheral vascular diseases when they have been employed at the same time that the patient was put at complete rest, made to abstain from smoking, given soaks and wet dressings and allowed to take alcohol by mouth. Any or all of these factors are capable of markedly influencing the therapeutic response. In addition, the factor of seasonal variation is frequently neglected. Vascular diseases (with the exception of erythromelalgia) usually tend to respond favorably to warm weather, so that if, for example, cases of Raynaud's syndrome or thromboangiitis obliterans are treated, the factor of environmental temperature trend may play a role in the picture.

Failure to consider these factors has frequently necessitated a complete revision of the original conceptions of the value of a therapeutic agent. This paper has been presented with careful consideration of this aspect of the problem, but I should like to emphasize the fact that even under these conditions it is highly probable that further re-evaluation will take place during the next ten years.

400 Madison Avenue

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## A POSTOPERATIVE FOLLOW-UP STUDY OF FOUR HUNDRED AND SIXTY-NINE THYROID PATIENTS

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IN 1934, a follow-up study of 303 thyroid patients was reported from this clinic.<sup>1</sup> Those cases had been observed after subtotal thyroid

which operation was performed from January, 1932, to January, 1937.

The definition of the term "thyrocardiac" given in the previous report is as follows: a patient with hyperthyroidism who has persistent auricular fibrillation or flutter up to the time of operation, or congestive heart failure with or without regular heart rhythm or both. Data concerning associated findings are given in Table 1.

It is not the purpose of this report to discuss in detail the pathologic physiology of the heart in hyperthyroidism. A review of this subject has recently been made from this clinic.<sup>2</sup> We wish to point out again, however, the fundamental difference between congestive heart failure due to hyperthyroidism on the one hand and congestive heart failure from intrinsic heart disease on the other. The heart fails in the former because of its inability to maintain circulatory needs for increased bodily metabolism, and in the latter because it cannot maintain circulatory needs for a normal bodily metabolism. The superimposition of auricular fibrillation in either group greatly adds to the heart's inefficiency. These relations are diagrammatically presented in Figure 1

### FIRST GROUP (1922-1932)

The majority of these patients were seen in the clinic during the five-year period following operation. Thereafter, contact was made mostly by questionnaires, which were frequently completed by the patient's physician. In 1932, the final out-

TABLE 1 Miscellaneous Clinical Data as Recorded in 469 Thyrocardiac Patients

CLINICAL FINDING	NO. OF CASES
Mitral stenosis, exclusive of cases with a rheumatic history	27
and apical systolic murmurs	1
Aortic regurgitation (rheumatic)	2
Aortic stenosis (rheumatic)	1
" "	1
" "	1
Aortic pericarditis (?)	1
Pericarditis	1
Interventricular block	1
Regular rhythm	2
Auricular fibrillation	2
Auricular flutter	2
Paroxysmal tachycardia	2
Coronary disease	2
Coronary disease, with auricular fibrillation	2
Cardiac asthma	1
Pulvus alternans	3
Asthmatic bronchitis	2
Severe anemia	9
Postoperative angina	1
Hypertension (160/90 basal or greater)*	3
Postoperative	36
Present since operation	15
Diabetes at or since operation	14
Postoperative myxedema	
Transient	
Permanent	

\*Includes only the 166 cases in the second group

ectomy over a period of one to ten years. Excellent results and a low operative mortality were demonstrated. The present report concerns a further follow-up study of the same group, and in addition, the present state of 166 cases in

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come was determined in 84 per cent, whereas in 1938 and 1939, 83 per cent were followed (Table 2).

Mortality

In 1934, the case mortality following operation was reported as 4.3 per cent.<sup>1</sup> Since that time, 13

formed elsewhere before the patients came under our observation. Thus, the probable operative mortality is about 3 per cent.

Sufficient time has not yet elapsed, nor has the number of cases been large enough, to permit the construction of accurate tables of life expectancy. However, a presentation of certain facts demon-

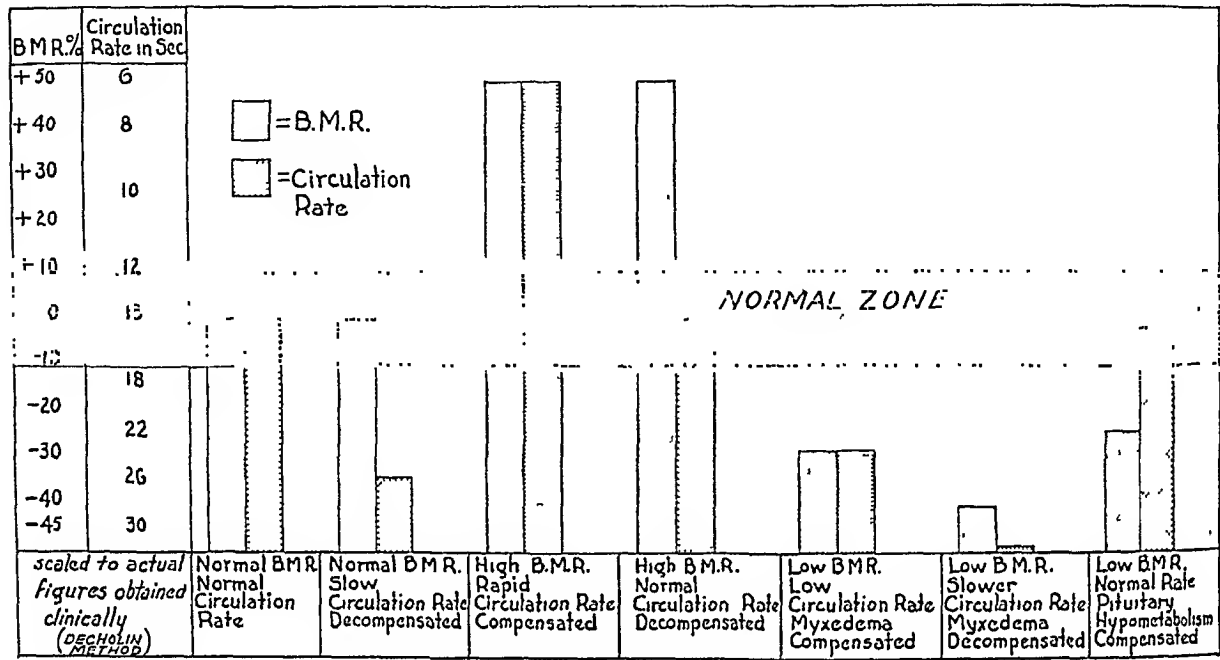


FIGURE 1. Relation of Circulation Rate to Metabolic Rate in Various Types of Thyroid Disease and Hypometabolism.

The data are based on clinical observations of circulation times (arm-to-mouth method, with decholin) and basal metabolic rates. The thyrocardiac patient with congestive failure is represented in the fourth column, with elevated basal metabolic rate and normal circulation time; this should be compared with the findings for the patient with ordinary congestive failure (second column).

of this group of patients have been reoperated on, with 2 deaths, the total mortality following operation being 5.0 per cent.

TABLE 2. Follow-Up Data on Patients in the First Group.

DATA	FOLLOW-UP IN 1933*	FOLLOW-UP IN 1939†
Number of cases operated on	303	303
Number of cases traced	256	252
Number of patients living.	208	164
Number of patients living who had congestive heart failure		104
Number of patients dead (including operative deaths)	48	88
Number of patients living, with regular heart rhythm . . .	149	122
Number of patients living, with auricular fibrillation. . .	56 (27%)	42 (25%)
Subsequent reoperation because of recurrent hyperthyroidism and congestive failure (2 operative deaths) . . . . .		2

\*One to ten years.  
†Six to sixteen years.

A little more than five hundred operative procedures were carried out on these 303 patients, including an estimated nineteen operations per-

strates the outcome to the present time. If the number of years that the patients were expected to live are totaled, the average for those who died after having survived operation is seventeen years. Actually, these patients lived only an average of six years; only 1 patient lived out his life expectancy. Of the total now living, only 6 have lived beyond their expected term of life, and the rest have still not reached their predicted span of life. Figure 2 shows the average expectancy of each year group up to and including 1928, and the number of years actually lived to date. These fall short of life expectancy, and it is doubtful if the group living at present will make up the discrepancy.

Figure 3 shows the present status of these patients. The numbers now alive, dead and untraced are easily seen. Since 1926, the majority are still living, but before that time the majority were dead. It probably may be assumed that the same proportion of those alive and dead exists among the untraced patients. Figure 4 shows what is known about patients who could not be



traced at this time. It depicts the number of patients lost track of during any year following operation and the number of patients followed for twelve or more years until last heard from, and also the number who lived for various intervals following operation.

#### *Persistent or Recurrent Hyperthyroidism*

Up to the time of this follow-up, hyperthyroidism recurred in 27 cases at various intervals

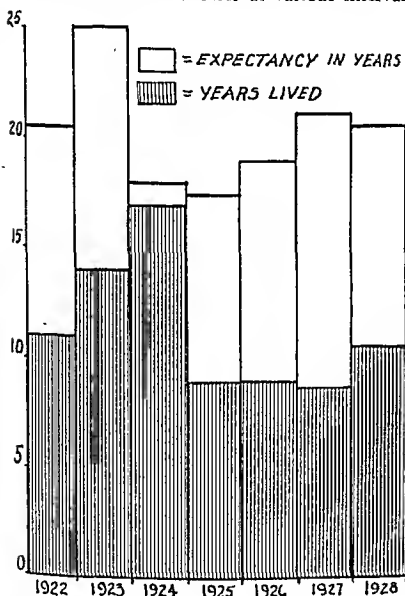


FIGURE 2. *The Average Expectancy in Years and Average Years Lived by Thyrocardiac Patients.*

*The number of years lived to date is shown in the cross-hatched areas, and falls short, by half, of the natural expectancy. The small number of cases in each group does not permit accurate conclusions, but the trend is distinctly abnormal.*

following operation. It is not always possible to decide whether a patient has persistent or recurrent hyperthyroidism, but of these, 6 might be said to have had persistent hyperthyroidism; the remainder had recurrent hyperthyroidism. Recurrence developed as long as ten years after operation. Of the 14 who were reoperated on, 3 died postoperatively (1 included in the former mortality figures), and 10 have so far remained well, or were well until they died; in 1, the disease has persisted and the patient is still taking Lugol's solution. Five patients were given x-ray treatment; 4 are still well, and 1 has not been

traced. Six patients were well controlled on Lugol's solution; 4 were not, and they were given roentgen-ray treatment as mentioned above. Of the total group, 6 are dead, 3 untraced, and 6 alive.

To determine the percentage of recurrent or persistent hyperthyroidism following subtotal thyroidectomy is at best a difficult problem. Many factors are involved, such as adequate or inadequate surgery, the length of time followed, the accuracy of the initial diagnosis, the type of goiter and the method of computing the percentage. To say that a certain number of patients have recurrences within a five-year period does not mean that the chance of recurrence is ended. Considered from the point of view of the whole life history of these patients, the final estimate of recurrence cannot be made until that history is complete.

Of the 303 patients operated on in this group, 41 have had to have secondary operations or other methods of controlling hyperthyroidism up to the present time. Nineteen of the 41 were operated on before they were first seen in the clinic. It is true that some of these patients may have had inadequate surgery, especially since the operations were done between 1917 and 1925; nevertheless, they must be included.

If these 19 cases, as well as the postoperative deaths and 51 untraced cases, are excluded, there remains a total of 221 cases from which the percentage of recurrences can be computed. Hyperthyroidism developed in 22, making a percentage of 10. In the 221 cases, 71 patients have died since operation. Of those dead, 4 were known to have hyperthyroidism (2 postoperatively); there is thus a known recurrence in 18 of 154 living patients, or 12 per cent for this particular group of patients with hyperthyroidism. The final percentage of recurrence cannot be accurately foretold, therefore, until these 154 patients have all died, which may require another ten years or more of observation.

This experience with recurrent or persistent hyperthyroidism, along with consideration of the 19 patients who had been operated on before coming under our care and who fell into the thyrocardiac group because of either insufficient surgery or a persistent or recurrent hyperthyroidism, illustrates that serious consequences may occur if patients are allowed to drift along with what seems to be mild hyperthyroidism. If the disease is mild, some may be controlled with iodine, but they must be followed carefully and operated on again if necessary. It seems probable that 2 patients who died postoperatively from recurrent hy-

perthyroidism could have been saved had they submitted to operation before severe heart failure and moderately severe hyperthyroidism developed. The degree of hyperthyroidism does not always foretell whether fibrillation or heart failure will subsequently develop. The diminished cardiac reserve in many of these cases, because of degenerative or other types of heart disease, cannot withstand at times even the burden of mild degrees of thyroid overactivity without loss of compensation.

*Auricular Fibrillation*

In the original group, there were 262 cases of fibrillation. Quinidine was used in 64 cases and was successful in restoring normal heart rhythm in 52. At the 1932 follow-up, there existed 56 cases of persistent auricular fibrillation. At the

and in the other spontaneously after the withdrawal of thyroid. The presence of auricular fibrillation after operation did not appear to shorten life as judged by the fact that 27 per cent of the patients alive in 1932 and 25 per cent of those alive in 1938 had auricular fibrillation. Most of these patients are taking daily rations of digitalis.

Recurrence of congestive heart failure is rare in the absence of coexistent organic heart disease, such as mitral stenosis. It developed a second time in 4 cases, owing to recurrence of hyperthyroidism.

*Causes of Subsequent Deaths*

Twelve patients were said to have died of heart disease; 11 died from either cerebral hemorrhage

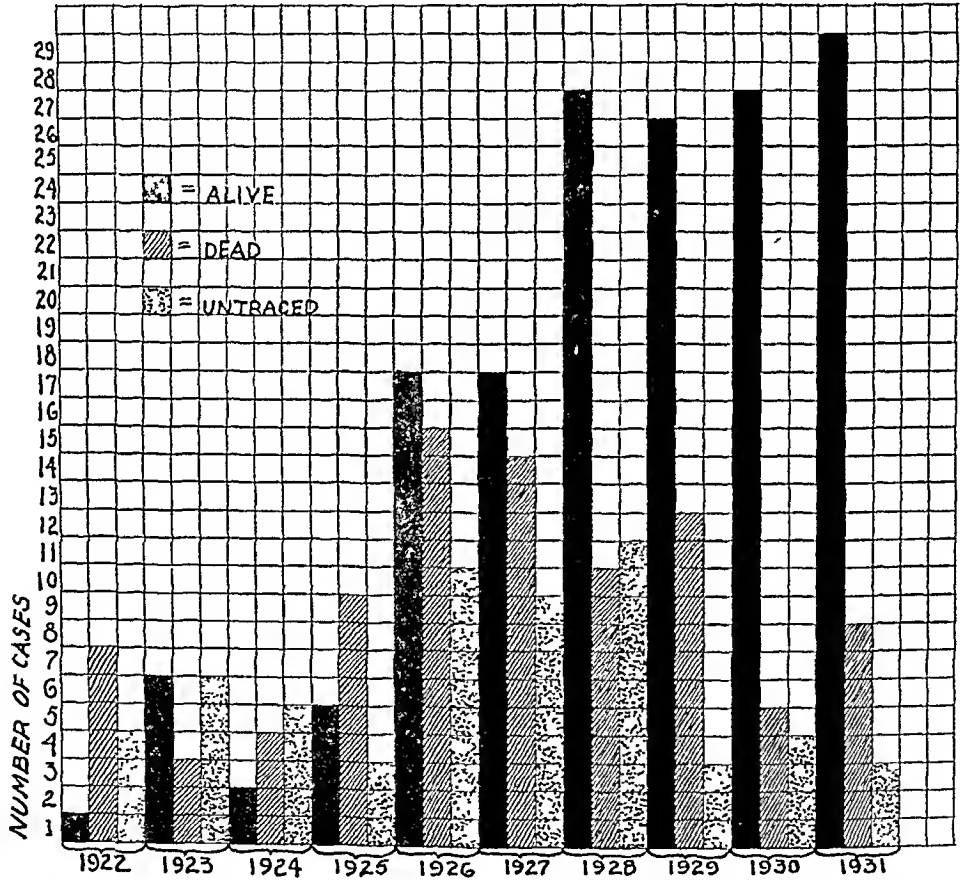


FIGURE 3. *The Number of Living, Dead and Untraced Patients in Each Year Group.*

present writing, 42 cases probably exist. In 5 cases in which the heart rhythm had been restored to normal, auricular fibrillation again developed without a known recurrence of hyperthyroidism, whereas 4 other patients returned with auricular fibrillation caused by recurrence of hyperthyroidism. Recurrence of auricular fibrillation took place in 2 cases with the administration of thyroid for mild postoperative myxedema, but normal rhythm was quickly restored—in one by the use of quinidine

or embolus when auricular fibrillation was present. It is difficult to assign the cause of these deaths accurately, but embolus seems the likeliest possibility. One patient died of mesenteric embolism. Four died of cancer, and in many the cause was not determined.

*Present Condition of Health*

An attempt to grade results is at best difficult and is not entirely satisfactory. Infirmities of age

and the presence of some unrelated disease, along with our inability to examine a good many of the patients personally, are some of the reasons why an accurate statement regarding results at the time of follow up is impossible.

In 111 cases, the rhythm is regular, and the patients are in good health, in 33, auricular fibrillation is present, but the patients are otherwise in

### Mortality

The case mortality in this group was 47 per cent. For the two groups, a total of 469 cases, the case mortality from operation is 4.5 per cent.

Fifty four one stage operations, 94 two stage operations, and 17 three stage procedures (two hemithyroidectomies and a pole ligation) were carried out, this makes a total of 293 operative

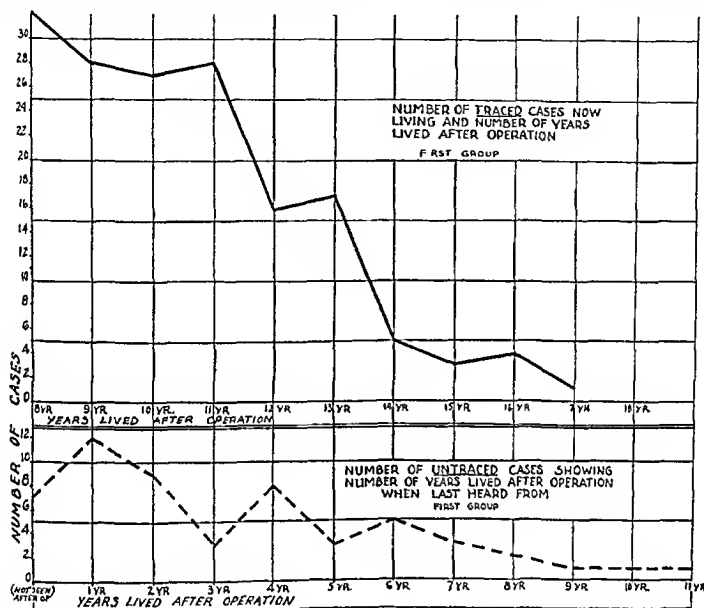


FIGURE 4 Data on Survival of Traced and Untraced Patients  
Although the number of patients operated on in 1922, 1923 and 1924 was relatively small  
the trend drops sharply after eleven years

good health, and in 20, the patients are in poor health from diverse causes, either auricular fibrillation or regular rhythm being present.

### SECOND GROUP (1932-1937)

The recent group of 171 thyrocardiac cases (1932-1937) is summarized in Table 3. One fact stands out in comparison to the first group, namely, that the number of cases of congestive heart failure seems to have decreased in relation to the number of cases of established auricular fibrillation. A little more than a third in this group had definite congestive failure as compared with more than half of those reported in the first group. The probable explanation is that these cases are being recognized or that the patients are being advised to have operation earlier than formerly.

procedures and thus gives an operative mortality of 27 per cent.

### Persistent or Recurrent Hyperthyroidism

Four of the 166 patients operated on had had a previous thyroidectomy. In 5 of these cases, hyperthyroidism recurred, 3 patients were reoperated on, and 2 are taking Lugol's solution. The incidence of recurrence to date in these cases is low, but sufficient time has not elapsed to permit a comparison with the first group.

### Auricular Fibrillation

Twenty four per cent of those traced and alive still have auricular fibrillation, as compared with 25 per cent in the first group. Quinidine sulfate was used in 33 cases, and in 20, normal rhythm developed during its administration. In some cases

in which quinidine fails to restore normal rhythm shortly after operation, a spontaneous return to normal may occur at a later date. Four such

TABLE 3. *Data on Thyrocardiac Cases Admitted from 1932 to 1937.*

DATA	NUMBER OF CASES					
	1932	1933	1934	1935	1936	TOTAL
Total . . . . .	40	25	36	35	35	171
Operated on . . . . .	37	25	35	34	35	166
Auricular fibrillation. . . . .	36	23	34	33	34	160
Auricular fibrillation with congestive heart failure. . . . .	10	6	12	8	15	51
Normal rhythm with congestive heart failure . . . . .	4	2	2	2	1	11
Operative deaths. . . . .	0	2	1	3	2	8
Subsequent deaths . . . . .	5	4	2	2	1	14
Survivals . . . . .	25	15	30	27	31	128
Untraced . . . . .	7	4	2	2	1	16
Normal rhythm at present . . . . .						98
Auricular fibrillation at present . . . . .	6	6	1	5	12	30
Recurrent hyperthyroidism. . . . .	2		1	2	0	5
Myxedema . . . . .	3	1	0	0	2	6
Reoperations . . . . .	1		1	1		3

cases were noted in this group. On the other hand, in our earlier experience, normal rhythm

perthyroidism or myxedema occurring at three months. As can be seen, the largest number of cases before operation had a metabolic rate between +30 and +40 per cent, and after operation a rate of between +10 and -10 per cent.

SUMMARY

Four hundred and sixty-nine thyrocardiac cases in which operation was performed from 1922 to 1937 have been followed. In the first group of 303 patients operated on between 1922 and 1932, 164, or 54.1 per cent, are living; 122 have normal heart rhythm, and 42 continue to have auricular fibrillation. Of the second group of 166 operated cases, 128 patients are still living, 98 of whom have normal heart rhythm.

The case mortality was 4.5 per cent, and the operative mortality was slightly less than 3.0 per cent.

The incidence of recurrent hyperthyroidism in

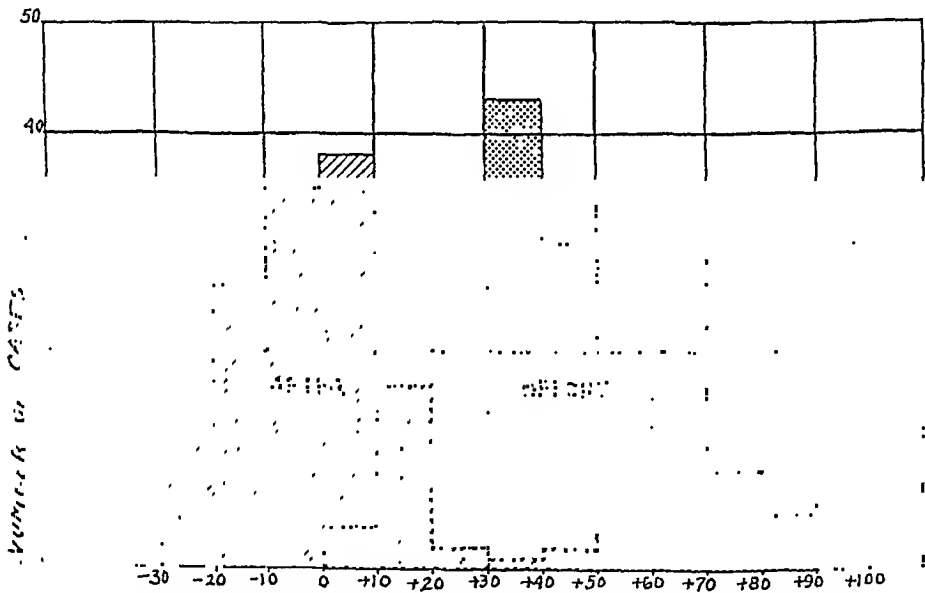


FIGURE 5. *Basal Metabolic Rates before and Three Months after Operation.*

was not infrequently restored in patients who had persisted in having auricular fibrillation two and three years after operation.

In this group, 1 case of hemiplegia followed the use of quinidine and restoration of normal rhythm, whereas 3 cases of embolism (1 pulmonary and 2 cerebral) followed operation on patients who had not been treated with quinidine.

Basal Metabolism

A comparison of the basal metabolic rates before and three months after operation is given in Figure 5. These include all cases of persistent hy-

perthyroidism or myxedema occurring at three months. As can be seen, the largest number of cases before operation had a metabolic rate between +30 and +40 per cent, and after operation a rate of between +10 and -10 per cent.

Although these patients are restored to normal activity for the most part, their expectancy of life based on the present follow-up falls considerably short of the predicted expectancy.

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## POLLEN DISEASE IN THE ABSENCE OF POSITIVE SKIN TESTS\*

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THERE is a small but distinct group of patients who, with the advent of the spring, summer or fall, suffer from characteristic bronchial, nasal or ocular symptoms, reminiscent of pollen disease, but who on skin testing fail to react to any of the prevailing pollens and molds.<sup>1,2</sup>

That these symptoms are due to some atmospheric inhalant, most probably pollens, is suggested by the fact that they recur each year, during a well defined pollen period, and cease when this period is over. In addition, the intensity of the symptoms varies directly with the extent of pollen pollution in the air.

In further support of this hypothesis is the fact that when patients in this group are placed in air filtered rooms, or when they change residence to a new locality with a different pollen flora, they are relieved. Most important, however, is the observation that these patients respond satisfactorily to specific pollen therapy, and in some cases even systemic reactions occur in the course of treatment. Such therapeutic results and the concomitant systemic reactions are possible only when patients are specifically sensitive to the substances injected.

What these patients lack to fulfill the criteria of pollen disease is positive skin tests. In some cases this lack seems only relative, since suggestive endermal reactions may be obtained with pollen extracts in high concentration, high potency extracts, however, often produce false positives, thus minimizing the value of the tests. In others, the more delicate ophthalmic<sup>3</sup> or nasal<sup>4</sup> tests, performed with dry, unaltered pollens, may give a clue to the correct diagnosis. But even these tests bear no constant relation to the symptoms. The only rational approach to this problem seems to be the history of the case, backed by a knowledge of the prevailing atmospheric flora during the respective seasons of the year, and a proper appraisal of the presenting symptoms.

The presenting symptoms in this group merit particular mention. In patients with bronchial complaints, wheezing may be absent or slight, the chief difficulty being either a harassing cough or complete apnea. Many patients become refractory to adrenalin and fall into a state of complete physical exhaustion bordering on collapse.

Those suffering from nasal symptoms complain more of stuffiness than of sneezing, and their chief difficulties are constant blowing of the nose and a sense of suffocation, particularly at night. The so called "ocular" group suffer from severe itch, altogether out of proportion to the local conjunctivitis. In general, severity characterizes the symptomatology in this group.

The incidence of negative skin tests to pollen has been variously estimated at between 2<sup>1</sup> and 13 per cent<sup>2</sup> of the total cases of hay fever.

During the last few years, I have observed 28 such patients, or about 7 per cent of the total pollen cases treated. Eleven of these, or 39 per cent, suffered from asthma, and a similar number from hay fever. Three, or 11 per cent, had cough as the chief complaint, and 3 others had conjunctivitis.

An evaluation of the clinical characteristics of allergy in this group reveals an incidence of positive family history, past history of allergy and

TABLE 1 Findings in 28 Allergic Patients with Negative Skin Tests

FINDING	NO. OF CASES	PER CENT
Family history of allergy	19	68
Past history of allergy	7	25
Blood eosinophilia	5	18 (average)
Positive ophthalmic tests	2	7
Positive nasal tests	4	14

blood eosinophilia comparable with similar findings in other types of human hypersensitiveness (Table 1). In the absence of positive skin tests, the results of the more delicate ophthalmic and nasal tests are recorded.

Contrary to what might be expected in this group, the incidence of positive ophthalmic tests was higher than that of nasal tests when performed with dry pollens. This close relation between the ocular mucosa and the shock organ merits further investigation.

Nineteen of these patients,—12 with asthma, 6 with hay fever and 1 with cough,—who were followed for a year or longer and who received the benefit of close supervision and treatment, were the subjects of the present report. There were 9 males and 10 females, with an average age of thirty-seven years. The average age at the onset of symptoms was thirty years, which is somewhat higher than the expected average in frank hay fever.

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In practically all cases, the symptoms extended over more than one pollen season: 9 patients complained of symptoms in spring, summer and fall; 6 in summer and fall; 3 in spring and summer; and 1 in spring and fall. This, again, is unlike the events in frank pollen disease, in which a single pollen sensitivity generally prevails. Evidently, aside from the fact that skin tests show these patients to be refractory, as a group they have other characteristics as well.

The management of these cases and the selection of pollens for treatment present a definite problem. In the absence of positive skin tests as a guide, one must draw chiefly on the history of the case and on experience with allergic patients whose skin tests are positive. On this basis, patients having symptoms during May and early June were considered sensitive to tree pollens, of which oak and birch are most important. Lesser offenders among the trees, such as elm, poplar, ash, hickory and others, were omitted from consideration because the periods of pollination are short, the dates overlapping in many cases, and because the amounts of pollen shed are comparatively small.

Patients suffering from early June to the middle of July were considered sensitive to grass pollens, and those having fall symptoms, from the middle of August to October, were designated as ragweed cases.

Other atmospheric offenders that prevail during the various pollen seasons and must be reckoned with are molds, particularly *Alternaria*, *Hormodendrum* and *Aspergillus*. Since the exact dates of their pollution in the air are not well defined, and in the absence of positive skin tests, their etiologic significance could not be determined.

Pollen dosage presents another problem for consideration. Most of these patients can tolerate large doses without any untoward reactions. Others, however, may have systemic reactions even from a small dose. Therefore, caution rather than experience is required in selecting the proper dose for the individual patient. Contrary to the procedure followed in frank pollen disease,—in which treatment is initiated with comparatively high dilutions and the doses are increased by 0.05 or 0.10 cc.,—in the nonreacting pollen group, the technic is somewhat different. The following is presented as a working basis, which, however, must be flexible in conformity with the individual needs of the patient:

Initial dose	0.1 cc. of a 1:500 dilution
Second dose	0.1 cc. of a 1:100 dilution
Third dose	0.1 cc. of a 1:30 dilution
Fourth dose	0.1 cc. of a 1:20 extract.

All further increases are made from the 1:20 extract until an arbitrary final dose of 1.0 cc. is reached.

Throughout the treatment, watch must be kept over possible systemic reactions; when these occur, the need of a more gradual increase in dosage and of a possible smaller final dose becomes apparent.

Since in the earlier cases a 1:10 pollen extract was used, for which the equally potent 1:20 extract was later substituted, all pollen doses were for convenience calculated on a 1:10 scale.

Table 2 is descriptive of the symptomatology, type of pollens, number of doses, the size of maximum dose and the results of therapy in each case.

TABLE 2. *Therapy and End Results in 19 Treated Patients.*

CASE No.	SYMPTOM	POLLENS	MAXIMUM DOSE (1:10) cc.	TOTAL No. OF DOSES	RESULTS
1	Asthma	Tree and grass	0.20	20	Good
2	Asthma	Tree and grass	0.75	21	Good
3	Cough	Grass and ragweed	0.65	22	Good
4	Asthma	Tree, grass and ragweed	0.40	24	Good
5	Hay fever	Tree, grass and ragweed	0.70	27	Good
6	Asthma	Tree, grass and ragweed	0.60	27	Good
7	Asthma	Grass and ragweed	0.85	29	Good
8	Asthma	Tree and ragweed	0.60	31	Good
		Averages	0.59	25	
9	Hay fever	Grass and ragweed	0.10	18	Fair
10	Hay fever	Grass and ragweed	0.50	20	Fair
11	Hay fever	Tree, grass and ragweed	0.70	27	Fair
12	Asthma	Tree, grass and ragweed	0.90	31	Fair
13	Hay fever	Tree, grass and ragweed	0.60	32	Fair
14	Asthma	Tree, grass and ragweed	0.45	35	Fair
15	Asthma	Tree, grass and ragweed	0.75	36	Fair
		Averages	0.57	28	
16	Asthma	Tree and grass	0.30	10	Poor
17	Hay fever	Tree, grass and ragweed	0.30	13	Poor
18	Asthma	Grass and ragweed	1.00	27	Poor
19	Asthma	Grass and ragweed	0.20	28	Poor
		Averages	0.45	20	

In addition, the average size and number of doses for patients with good, fair and poor results from treatment are included at the bottom of the respective columns. The estimation of end results in pollen therapy on the scale of good, fair or poor has been adopted because of its simplicity and fair amount of accuracy.

Table 2 shows further that patients with good and fair results received a higher average number of pollen doses and larger final doses than patients with poor results. This suggests a possible causal relation between the intensity of treatment and the end results. At the same time, patients who failed to obtain satisfactory results had a higher incidence of systemic reactions than those whose responses to therapy were more favorable (Table 3). These figures suggest that patients with poor results have a higher degree of "shock organ" sensitivity, and that with some modification in the

technic, improvement in this group may not be impossible.

Altogether, 15 of the 19 patients, or 79 per cent, were benefited by the treatment. These figures are impressive and emphasize the merits of

TABLE 3. *Results of Treatment in Relation to Systemic Reactions.*

RESULT OF TREATMENT	NO. OF CASES	SYSTEMIC REACTIONS	
		NO. OF CASES	PER CENT
Good .....	8	2	25
Fair .....	7	1	14
Poor .....	4	2	50

pollen therapy in patients whose skin tests are negative.

### DISCUSSION

The group as a whole is presented to illustrate a type of allergy that is masked by a lack of positive skin tests. However, the clinical characteristics of these patients—their symptomatology, their aptitude for allergy, their response to specific therapy and, finally, their tendency to systemic reactions from an overdose of pollen extract—leave no doubt that their etiologic group-*ing* is correct.

The important factor in this group is the seasonal incidence of the disease. The general tendency would be to place such patients among the undiagnosed or intrinsic cases whose symptoms are due to causes from within the body, but the proper appraisal of the disease opens an approach to specific therapy that promises some degree of success.

An example of such success is the patient in Case 2, whose seasonal asthma confined her to her bed each spring for a period of from six to eight weeks, but who has remained well with specific treatment; another example is the patient in Case 5, who was similarly affected each summer, but who has lost no time from work since treatment began. In Case 7, the patient collapsed and was in a state of unconsciousness in July, 1939, because of severe asthma, and was saved only through heroic treatment with adrenalin, an oxygen tent and so forth. In 1940, under pollen therapy, he had two mild attacks, which required no adrenalin. In these three cases, nasal and ocular tests to the offending pollens were negative.

The occurrence of clinical symptoms from the inhalation of small quantities of pollen in the air, in spite of negative ophthalmic or nasal tests, defies explanation.

Of particular interest is Case 3; for twenty years, the patient had had an intractable summer cough, lasting from the middle of June until the fall. Skin tests were negative, and ophthalmic tests doubtful. Treatment with extract of timothy and ragweed brought complete relief. In this case, cough was the presenting symptom, and pollens were the cause.

The occurrence of so many constitutional reactions (in 6 out of 19 patients) seems inexcusable, except that in the past, I have vainly attempted to treat similar patients with smaller doses. It was only in desperation that stronger doses were used, and only on the assumption that when skin tests are negative, the tolerance for pollen is high. In a measure, this is true, but it is also true that the shock organs, particularly the bronchi, have their own measure of tolerance, regardless of the response of the skin. The question then arises, What can be done to avoid such reactions? No definite answer can be suggested except the cautious increase of each successive pollen dose as treatment progresses. The local reactions to the injections in this group were few, often delayed in onset, and occurred only with doses close to 1.0 cc. of the extract. But even in these cases, the local reactions bore no relation to the systemic reactions, most of which occurred in the absence of local reactions.

Another point that merits discussion is the number of doses injected in each patient. Many of those in dilutions higher than 1:500 were undoubtedly superfluous. Yet, it is possible that the summation of the repeated injections ultimately bore results. Thus, in treating these patients, one may omit the lower dilutions, and safely start with a 1:500 extract. Beyond this, the advances must be cautious, and experience alone must be the guide in estimating further doses.

No explanation can be offered for the failures, particularly in those patients who experienced constitutional reactions. Evidently, the pollens used were specifically indicated, the dosage was carried to the point of tolerance and even higher, and yet the results were poor. The only consoling thought is that failures also occur in skin-sensitive patients, in spite of the most intensive treatment; however, in the skin-negative group the percentage of failures was higher.

In the final analysis, the mechanism of relief in pollen therapy is not clear, although the discovery of the blocking antibody in the serum of treated patients offers some ground for speculative thought.<sup>8</sup> Pollen therapy is justifiable chief-

ly on the basis of so many excellent clinical results. By the same token, it seems reasonable to treat the refractory group with pollen extracts if the history points to pollen disease. The broader application of these observations must find its way to the large number of patients with perennial allergy, who, in the absence of positive skin tests and lacking the seasonal element, present a difficult problem both in diagnosis and in treatment.

### SUMMARY AND CONCLUSIONS

Pollen disease in the absence of positive skin tests presents a definite problem in diagnosis and treatment.

A knowledge of the atmospheric flora in a given locality and of the dates of pollination makes a correct diagnosis possible.

Treatment given with corresponding pollen extracts offers relief in a high percentage of cases.

The technic of treatment is outlined, and the incidental systemic reactions are pointed out as possible complications.

Several characteristics of patients with negative skin tests are described, and emphasis is placed on the severity of their symptoms.

371 Commonwealth Avenue

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## NEW HAMPSHIRE MEDICAL SOCIETY

### PROCEEDINGS OF THE ONE HUNDRED AND FIFTIETH ANNIVERSARY

May 13 and 14, 1941

TUESDAY, MAY 13

THE scientific session of the New Hampshire Medical Society was opened at the Hotel Carpenter, Manchester, at two-thirty o'clock in the afternoon, with President Ezra A. Jones presiding.

Three papers dealing with fractures were presented, as follows: "Fractures of the Forearm and Humerus," Dr. Augustus Thorndike, Jr., Boston; and "Femoral Fractures," Dr. George W. Van Gorder, Boston; and "Fractures of the Foot and Ankle," Dr. Otto J. Hermann, Boston. This was concluded by a talk, "Glaucoma," by Dr. Paul A. Chandler, Boston.

WEDNESDAY, MAY 14

The morning session convened at eleven o'clock, with President Jones presiding.

The following remarks were made by the visiting delegates from other New England state medical societies:

DR. FRANK R. OBER, Boston: It is a pleasure to be here with you, and I bring the best wishes of the Massachusetts Medical Society to the New Hampshire Medical Society.

I am going to say only a word, which has to do with postgraduate teaching. A few years ago, the Massachusetts Medical Society established the New England Postgraduate Assembly, for the benefit of all doctors in New

England; your state, Maine, Vermont and Rhode Island voted to join the assembly, and last year Connecticut came in. Incidentally, Connecticut has conducted a clinical congress for a great many years—I think next year will be the sixteenth. I know of only one other state—Kansas—that has had meetings of this type for a longer period.

The program committee represents the hospitals and medical schools of Boston, the different states and the members of the assembly. The speakers are from outside Boston, and are chosen because they are outstanding in their fields of medicine.

The next meeting will be held on October 29 and 30. Last year, we had it in the middle of November, and it rained cats and dogs for the two days; the year before, it rained cats and dogs the first day. This year we hope for better weather.

We charge a fee that is supposed to cover the general expenses and those of getting the speakers; last year, however, we lost over \$600.

The meetings are held in Cambridge, at the Sanders Theatre, in Memorial Hall, Harvard University. We believe the assembly should be an entirely scientific affair; hence, there are no exhibits of any sort.

I hope that all of you will act as spark plugs in your district or county societies, and urge as many members to come to the next meeting in October as possible.

DR. WILLIAM T. ROWE, Rumford, Maine: The Maine Medical Association sends hearty greetings to the New Hampshire Medical Society at its one hundred and fiftieth annual meeting, and best wishes for a successful gathering.

You are, indeed, fortunate to be able to secure for your meetings some of the leaders of the medical world. Last year, as the Maine delegate, I had the pleasure of listening



to the president of the American Medical Association here in this auditorium, and today I hope to have the added pleasure of listening to the new president of the American Medical Association, Dr. Frank H. Lahey of Boston.

The annual session of the Maine Medical Association will be held at the Marshall House, York Harbor, on June 22, 23 and 24. On Sunday evening, we are planning to have a guest speaker who has recently returned from England. Monday and Tuesday mornings, the system of conferences will be continued. Monday and Tuesday afternoons, there will be guest speakers from outside Maine. Monday evening, there will be a reception in honor of the President of the Association and his wife, Dr. and Mrs. Thomas A. Foster.

The Maine Medical Association congratulates you on your long and honorable record. We invite you all to be with us at York Harbor at our annual meeting.

Dr. ARTHUR B. LANDRY, Hartford, Connecticut. I bring you greetings and best wishes from the Connecticut State Medical Society on this, your one hundred and fiftieth anniversary. You may celebrate your past rightfully because it has been a notable and a dramatic one, full of achievements.

I congratulate you, and all the more do I congratulate you because inherent in your past is the urge and vision that must regard this celebration as only a pause and a breathing spell, before you gain further momentum for the unfulfilled account that lies before you.

It is, alas, true that many celebrations of the past be come deadly, nursing complacency and anesthetizing fresh endeavor and conflict. Henry Ward Beecher tells the story of the dog that, in its puppyhood, chased a squirrel up a tree until he came to a hole in the tree, and that he spent the rest of his natural life barking up the hole of this tree. But that is not true of the members of this society, and certainly it is not true of the medical profession as a whole.

In these times there are many changes that demand intelligence and generous tolerance. Never was the opportunity so great for advance, service and achievement. If there ever was a time to follow St. Paul's challenge in our profession it is now, we should forget the things that are beyond and reach forward to those before us. So, let us press on toward the mark of our high calling.

We, of the State of Connecticut, will celebrate our one hundred and fiftieth anniversary next year, in Middle town, where the first meeting of the Connecticut State Medical Society was held. We invite you all to come and see us at that time, and we assure you of a very warm welcome.

Dr. ARTHUR H. RUGGLES, Providence, Rhode Island. To this most auspicious and historical occasion, I bring greetings and very best wishes from the Rhode Island Medical Society.

It is a great pleasure for one who originated in New Hampshire to return. I sometimes think that those of us who were careless enough to wander away live for the opportunity to get back here. I know that I always get a real thrill whenever I set foot in this state.

Dr. Frank H. Matthews, also a former resident of New Hampshire, and the other delegate from the Rhode Island Medical Society, is ill and could not come. He sends his official greetings to your society and to his many friends in New Hampshire.

I bring to all the members of your society an invitation to attend the summer meeting of the Rhode Island Medical Society, which is to be held at the Viking Hotel,

Newport, on May 28 and 29. Any of you who can come will have a cordial welcome.

I shall say one other thing. It seems to be that on this historic occasion for your society, we ought to emphasize one fact, and keep emphasizing it, namely, that there never has been a time in the history of the world when physicians need to stand together more firmly than at the present. We all realize some of the problems of social revolution through which we are going, and the world needs our clear thinking, our careful decisions and our united action that is why it seems to me most fortunate that in all our gatherings we can have representations from the various states, and that together we can listen to the papers and discussions, and that we can always hold curbstone consultations with each other, so that we may know the thoughts of the various groups and try, in our actions and as we face a troubled and important future, to have the medical profession stand together and think clearly.

Dr. LUCIUS C. KINGMAN, Providence, Rhode Island. When our society was founded, your society was just old enough to vote. When it was rumored around Rhode Island that you were to have your one hundred and fiftieth anniversary, there was a little lifting of eyebrows. Then, it was intimated that probably you had to gather in all the Indian medicine men in the community to get enough men to make a society. But, when it was pointed out that Rhode Island did not sign up with the Union until a year after New Hampshire did, they thought possibly there was something in it.

I have still another invitation to bring to you. Dr. Ruggles has already extended the invitation to you to attend our annual meeting at the end of this month at Newport, but I am going to invite you to come to our one hundred and fiftieth anniversary in 1962.

General Bowen then spoke as follows:

I should not wish to have this opportunity pass without appearing before the members of the medical profession in this state to express my appreciation of the wonderful contribution that the physicians have made to the success of the Selective Service System.

As you know, the United States Army is engaged in selecting men on a different basis than was ever done before. These men are not intended to go in for one year's service only, but they are intended to pass into the reserves and remain men who are capable of good field service for ten years. In other words, we are trying to pick men so well that they can remain in storage for that length of time, and that explains why there is so much insistence on the work of the medical profession. It is through the medical service that these men are passing to make this army that we are establishing the best anywhere. In doing that in New Hampshire, we have the services of about one hundred and eighty-five medical officers, all serving without compensation, either as examining physicians or additional examining physicians, members of the medical advisory boards or somewhere else in the service, from the top to the bottom, from the Board of Appeal right down the line.

The amount of work that has been done by these men has been tremendous. Since the registration last October, they have made about 3500 examinations, and these have been detailed examinations, in the course of which they have rejected approximately 45 per cent of the selectees.

That means a lot of work, and destruction, in many cases, of the doctor's regular practice. But, I want to say publicly to all who are here that I have never heard

one complaint from any physician; in fact, some of them have been so interested in this work that they have not even asked for assistance of any kind. In some cases, we have had practically to force a physician to take another man to help him.

In passing, I should also like to mention that we have now arrived at an answer to the great medical problem of the deferment of physicians, of interns and of medical students. This will not be done in a blanket way, but each case will be considered by its local board; and since we will probably know the requirements of the United States Army within the next few months, by next fall you may rest assured that the ranks of the medical profession will not be depleted, nor will the steady flow of young men into the profession, which you need so badly, be interrupted.

On behalf of the National Director, on behalf of His Excellency, the Governor of this state, on behalf of the staff guiding the work of the Selective Service System in this state, and on my own behalf, I thank you all very much. I thank the president of the Society for his continuous co operation with us in every possible way, and I thank the physicians for the wonderful help that they have given.

I know that we all see that at this time, as in the past, the physicians are ready to make their contributions, both now in preparing an army, and later on the field, if, unfortunately, this great country should be obliged to enter the war.

Captain Wheeler added the following:

General Bowen has asked me to read a few figures concerning the defects that were found, which might be of interest to the medical profession. The figures are correct up to about a month ago.

As General Bowen has said, approximately 45 per cent of those examined were found unqualified for general military service. Some of these were found qualified for limited service, and the others were disqualified.

Of those rejected, about 28 per cent were thrown out because of defective teeth alone. Furthermore, 41 per cent of those rejected had teeth sufficient to reject them, but had other causes, also. But, one might say that, without any other causes, nearly 70 per cent were rejected because of their teeth.

Nine per cent of those rejected were thrown out solely because of eye defects, and about 5 per cent for hernia. Twelve per cent of those rejected had muscular skeletal defects.

A number of men were rejected for so-called "mental causes"—mental deficiency, as well as the psychoses. Over 5 per cent were rejected solely for mental conditions; however, 9.3 per cent of those examined were mentally deficient or mentally defective in one way or another.

The morning session was concluded by an address by Dr. Frank H. Lahey, of Boston, the title being "The Management of Lesions of the Stomach, Duodenum and Jejunum."

The afternoon session convened at two o'clock, with Vice-President Charles H. Dolloff, presiding.

The Secretary, Dr. Carleton R. Metcalf, gave a résumé of the actions of the House of Delegates, and Dr. Deering G. Smith, delegate to the House of Delegates of the American Medical As-

sociation and chairman of the Committee on Medical Preparedness of the Society, repeated, in part, his report as given to the House of Delegates of the Society.

The report of the Trustees was then presented by Dr. Henry O. Smith.

#### FINANCIAL REPORT OF THE TRUSTEES OF THE NEW HAMPSHIRE MEDICAL SOCIETY FOR THE YEAR ENDING MAY 13, 1941

##### Receipts

Interest on various deposits, other than Benevolence Fund ..	\$420.47
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##### Expenditures

Transferred to Benevolence Fund	\$1,000 00
Trustees of Dartmouth College	2,000 00
Pray and Burnham prizes	150 00

Total expenditures	\$3,150 00
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Decrease in funds, other than Benevolence Fund	\$1,729 53
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##### GENERAL FUND

Deposits: New Hampshire Savings Bank	\$5,754 05
Portsmouth Trust and Guarantee Company	3,470.76
Nashua Trust Company	1,672 50

Total funds available May 13, 1941	\$10,897 31
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##### BARTLETT FUND

Deposit: Portsmouth Savings Bank (\$352.11 of this is a permanent fund, the income to be "expended only for the benefit of medical science, as may be directed by vote of this society")	\$4,643 26
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##### PRAY FUND

Deposit: Strafford Savings Bank (\$1000 of this is a permanent fund, the income to be expended only for prize essays)	\$1,294 00
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##### BURNHAM FUND

Deposit: New Hampshire Savings Bank (\$1140 of this is a permanent fund, the income to be expended only for prize essays)	\$2,191.00
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##### BENEVOLENCE FUND

Deposit: New Hampshire Savings Bank (\$349.81 of this is accrued income available for the purposes of the fund)	\$4,224 50
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A prize of \$100 was awarded for a paper entitled "Scientific Medicine in General Practice" by "Edward L. Hale," pseudonym for Dr. Oliver S. Hayward, of New London, New Hampshire. It is expected that prizes will be offered in 1941-1942, and notice will be sent to the members of the Society in due time.

The accounts of the Treasurer of this Society have been examined and found correctly cast and properly vouched.

HENRY O. SMITH  
SAMUEL T. LADD  
FREDERIC P. LORD

Dr Stanley B Weld, of Hartford, Connecticut, then spoke concerning the National Physicians' Committee, and was followed by Dr Jones, who delivered the presidential address, entitled *Orthopedics in New Hampshire*. The scientific session was concluded by a talk, *'The Work of the Medical Examiner,'* by Dr William J Brickley of Boston.

The banquet was held at the Hotel Carpenter at six thirty o'clock, with Dr David W Parker, of Manchester, as toastmaster. Following the opening remarks of Dr. Parker, President Elect Charles H Dolloff, of Concord, and President Jones spoke briefly. Dr Harry H Amsden, of Concord, then gave an address, *"The Doctor of One Hundred and Fifty Years Ago"*. Dr Frederic P Lord of Hanover, spoke concerning the prominence of the Mussey family in the medical history of New Hampshire, and introduced William C Mussey, he then gave a short account of the equally prominent Smith family, and introduced Dr Henry O Smith, Dr Deering G Smith and Robert G Smith. Dr Henry O Smith, of Hudson, described the career of Dr Josiah Bartlett, the founder and first president of the Society, and introduced Mrs Levi S Bartlett and Mrs Lottie Goodrich the latter a direct descendant of the founder. Dr Marion Fairfield, of Nashua, then read the appreciation of Dr Bartlett pronounced by Dr Thomas W Luce, at the time of his retirement as president of the Society.

In passing out of the picture as the retiring president I want to use the time at my disposal in talking to you about the man who first held the office I am being relieved of today. It has long been the custom of most presidents of this society to refer to their predecessors in the office in some complimentary way. This seems to me a fitting thing to do because some very able men and, indeed, some very eminent men, have been presidents of this society. To my mind, however, no one in this long list of incumbents, covering the whole period of one hundred and thirty five years, has ever quite measured up to our first president, Josiah Bartlett.

His history is probably well known to most of you and its recapitulation at this time may seem trite. I have, however been led to select him as my theme tonight for two reasons. First, this happens to be the sesquicentennial of the Declaration of Independence, which he did so much to bring about, and next because I believe his story should be told here once in a decade or so by someone, lest we forget our great inheritance.

Josiah Bartlett, then, was born in Amesbury in 1729. At the age of sixteen, he went into the office of a relative, Dr Ordway, and began the study of medicine. This was some twenty years before our first medical school was established in Philadelphia, and physicians were made in those days just as carpenters and blacksmiths were made, by a five to seven years apprenticeship with a master.

Josiah had been well grounded in the three Rs and had a good elementary knowledge of Latin and

Greek, and he was a good student. He had the clinical advantages afforded by Dr Ordway's large practice and also the use of his very good library. He did a great deal of dissecting during the five years of his term with Dr Ordway, and he became a very proficient anatomist, also his notes on his study of plant life gave evidence of good knowledge in this field.

In 1750, when he was twenty-one years old, he settled in the town of Kingston and commenced a medical practice which he continued for forty five years. He was a close and careful observer and quite early in his medical career he discovered what he believed to be gross errors in the then accepted pathology and treatment of several diseases, and with a boldness which always followed his convictions, he inaugurated many medical reforms, some of which almost constitute marking stones of medical progress in New England. His crowning medical achievement from our view point, perhaps, was the founding of this society. He secured its charter, wrote its constitution and bylaws, and then, associating with himself eighteen other physicians of the state, all men of prominence in their profession, he formally organized this society on February 16, 1791. He was naturally made the first president, and was re-elected for four successive terms.

Quite early in life, he became interested in military affairs and gradually rose to be a colonel in the King's militia, and was at that time the highest ranking military officer in the state. His colonel's commission was recalled, and his house in Kingston was burned by a spy in 1774, because of his patriotic activities, but many of our New Hampshire soldiers who distinguished themselves under General Stark at Bunker Hill and Bennington, and at Burgoyne's surrender, and later under General Washington in the southern campaigns, received their military training from Colonel Bartlett.

While with Dr Ordway and during the early years of his professional life, he whiled away his spare time in reading law books. He somehow acquired a knowledge of the law, which, combined with his sound sense and judgment, was recognized in 1780 in his appointment as a justice in the Court of Common Pleas. In 1787, he was elevated to the Supreme Court of New Hampshire. When we recall the national reputations of some of the New Hampshire lawyers of his period, we have to believe that his standing as a justice must have been far from mediocre.

Josiah Bartlett frequently represented his town in the legislative assembly, and in 1775, he was elected to the Continental Congress. When the greatest state paper ever conceived by the mind of man came up for a vote of ratification, the roll was called by states—New Hampshire, the northernmost state, was called first and Georgia, the southernmost, last. Thus, Josiah Bartlett was the first member to vote yes for the Declaration of Independence, and after that document had been signed by the president of the Congress, John Hancock, the second to sign was Josiah Bartlett. This act has made him immortal, and yet it fell to his lot a few years later to render his country perhaps an even greater service. When the Constitution was submitted to the states, it encountered considerable opposition. It was necessary, if it survived, that nine states accept it. Eight had accepted it when our constitutional convention met in February, 1788, and as New Hampshire was the ninth state, the attention of the entire nation was directed to this assembly.

Josiah Bartlett, always a resourceful politician, was a member of that convention, and he ascertained quite early that the measure was bound to fail because so many of the delegates, particularly from the smaller towns, were under instruction to vote against it. He, therefore, secured an adjournment until the following June. He then began a very intensive personal campaign for the constitution and was rewarded, when the convention reconvened, by a 57 to 46 vote for its acceptance. So we may possibly owe to the energy and wisdom of Josiah Bartlett some of the greatly vaunted constitutional rights and privileges that we enjoy today.

New Hampshire was the first state to have a constitution of its own, and that constitution, under which we live and do business today, was very largely written by Josiah Bartlett. He was the first governor of the state under that constitution, and was re-elected for four successive terms. He was then elected a member of the United States Senate, but was unable to serve because of physical infirmities.

He brought up a family of twelve children. Three of his sons and seven of his grandsons became doctors of medicine.

All this I submit as a brief survey of some of the outstanding events in the career of a remarkable man.

Josiah Bartlett is described by his contemporaries as a tall man of fine figure, affable but dignified in his manner and very particular in his dress. He wore his auburn hair in a queue, a white stock at his throat, ruffles at his wrists, short clothes, silk hose, low shoes with silver buckles. One writer, the Rev. Dr. Rollins, describes his bearing as that of "an Athenian philosopher, fine and aesthetic, curiously mingled with Yankee shrewdness, cool and practical."

In Amesbury, the house in which he was born is owned and maintained by the Josiah Bartlett Chapter of the Daughters of the American Revolution. His bronze statue standing in the square was unveiled in 1888, and Whittier's poem, "The Signer," was written for the event. His picture hangs on the wall in our state house, and the town at the southern entrance to our beautiful Crawford Notch is named in his honor.

In the town of Kingston, on a slight elevation overlooking the village green, still stands the fine, old-fashioned house that he built and lived in, after his first house was burned in 1774. It has always been owned and occupied by his descendants. It is in a good

state of preservation and is literally filled with Josiah Bartlett's belongings. Its present mistress, Mrs. Levi S. Bartlett, is always glad to welcome anyone who may be interested and takes delight in showing the house and the doctor's things.

It seems to me that we, as members of this venerable society which he founded, as well as sons of the State and Nation which he helped to found, may well regard this fine old mansion as our particular shrine, to which we should feel in duty bound to make at least one pilgrimage, in humbleness of heart, and, as has been said by a former president, hope to gain from such an experience at least some degree of that rare devotion to our profession and to our country that characterized Josiah Bartlett.

Across the green from the house is the old tavern and in the rear of this is the village cemetery, in one corner of which a plain pile of cut granite marks the last resting place of the first president of this society. The inscription states that he died May 19, 1795, in the sixty-fifth year of his life.

And now, in closing, I want to read to you the last words of his message to this society as its retiring president. This was written and sent out from his sickroom in that old house in Kingston and was read at the annual meeting held in Concord in 1794. These words are, and perhaps were intended to be, as much a message for us of today, as they were for those members who listened to them as they were read, in this very place, one hundred and thirty-two years ago:

That the members of this Society may be useful to themselves and the public, and enjoy that exalted pleasure that arises from a consciousness that they have contributed to the health and happiness, not only of their patients, but, by communicating to others the knowledge and cure of disease, to the general happiness of the human race, is the ardent wish, Gentlemen, of your very humble servant, Josiah Bartlett.

Governor Robert O. Blood spoke concerning the increasing participation by the State in matters pertaining to medical care, and the program was concluded by Dr. Lahey, who recounted many of the current problems facing the medical profession in the United States.

## MEDICAL PROGRESS

### TREATMENT OF MENINGITIS<sup>6</sup>

MAXWELL FINLAND, M.D.,<sup>†</sup> AND JOHN H. DINGLE, M.D.<sup>‡</sup>

BOSTON

PRIOR to 1936, recoveries from acute bacterial meningitis due to organisms other than the meningococcus were quite rare, in spite of laborious and often heroic therapy of many sorts. The mortality in the meningococcal cases was likewise very high, in spite of the almost universal use of specific serums and other measures. The results reported<sup>1-3</sup> in several large series of cases are probably typical, although small groups of cases with more favorable results from various therapeutic procedures were occasionally reported.

Tripoli<sup>1</sup> summarized the results of different kinds of treatment at the Charity Hospital in New Orleans between 1925 and 1934. His series included 221 cases of meningococcal meningitis with a mortality of 65 per cent and 247 other cases of nontuberculous acute meningitis with only 3 recoveries. All the patients with meningococcal meningitis received antiserum intravenously and intramuscularly, but the lowest fatality rates (42 and 48 per cent) were obtained in those patients who received intraspinal and intracisternal injections in addition.

Lindsay, Rice and Selinger<sup>2</sup> reviewed 331 cases of meningitis treated at the Children's Hospital in Washington during the ten year period from 1924 to 1933. The mortality was 40 per cent in 58 cases of meningococcal infection, whereas only 3 patients recovered among 133 with other proved bacterial etiology after the tuberculous and the syphilitic cases were excluded.

Neal<sup>3</sup> summarized 3178 cases occurring in New York City during a twenty five year period prior to 1935. In this series, there were 829 cases due to bacterial agents other than the meningococcus or the tubercle bacillus, with only 24 recoveries. In an earlier paper, Neal and her associates<sup>4</sup> had reported 302 cases of meningococcal meningitis

for whose treatment they were responsible. These cases occurred during a five year period prior to 1931, and the mortality in this series was 18.3 per cent. Walsh,<sup>5</sup> however, estimated that the mortality from cerebrospinal fever in the United States from 1920 to 1936 averaged over 50 per cent.

As with most other serious acute bacterial infections, chemotherapy with the sulfonamide drugs has almost completely revolutionized the management and the prognosis in cases of acute purulent meningitis. The successes from chemotherapy alone have been so frequent and so striking by contrast with previous results that many of the specific therapeutic measures and other procedures formerly thought to be helpful and even essential are rapidly being discarded. In this report, we shall summarize the current opinions concerning the chemotherapy and specific serotherapy of acute meningitis due to some of the commoner bacterial agents, and shall consider the present status of some of the nonspecific therapeutic procedures previously employed. A more comprehensive review of the recent literature, particularly that dealing with meningococcal meningitis, has been prepared for publication elsewhere.<sup>6</sup> Keefer's<sup>7</sup> recent clinic also contains a summary of important features concerning the pathogenesis, diagnosis, prognosis and treatment of meningitis.

### GENERAL ASPECTS OF TREATMENT

#### *Meningococcal Meningitis*

Cerebrospinal fever has long been recognized as a "scourge of armies." This is due to the spectacular nature of the clinical manifestations and not to a high attack rate or to a high fatality rate. The disease usually strikes in an almost mysterious way, without warning, thus having a marked depressing effect on the morale of the military personnel.<sup>8</sup> During World War I, there were 5839 cases of meningococcal meningitis in the United States Army, with 2279 deaths.<sup>9</sup> The disease was also quite prevalent in this country during the late twenties, spreading from the West Coast through the Middle West, but tending to spare the cities of the Atlantic Seaboard.<sup>8</sup> In recent months, there have been a considerable number of

All articles in this series will be published in book form in the current volume of *Medical Progress*, Annals 1940 (Springfield, Ill.) no. 5. Charles C. Thomas Company 1941. \$4.00.

<sup>†</sup>From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard) Boston City Hospital and the Department of Medicine and the Department of Bacteriology and Immunology, Harvard Medical School.

This study was aided in part by a grant from the William W. Willington Memorial Research Fund, Harvard Medical School.

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cases in Nova Scotia,<sup>10</sup> and in Great Britain some 12,500 cases were reported during 1940.<sup>11</sup> Further outbreaks are likely to occur in this country in the near future.

**Chemotherapy.** Soon after the recognition of the effectiveness of sulfanilamide against the hemolytic streptococcus, Buttle, Gray and Stephenson<sup>12</sup> reported that this drug was also effective against meningococcal infections in mice. Since that time, sulfanilamide and several of its derivatives have been used widely and effectively in the treatment of cerebrospinal fever in human beings. Reliable figures of case fatality rates with chemotherapy alone are difficult to obtain, however, for several reasons: there were wide variations in mortality rates, both with and without serum, before the introduction of chemotherapy; from many of the reports, it is not possible to determine the number of cases receiving any one kind of therapy, and many patients received more than one kind of treatment; some of the fatal cases have often been excluded for a variety of reasons; data concerning the factors that influence the outcome have not always been presented in adequate detail. Nevertheless, it is abundantly evident that chemotherapy alone is highly effective in curing this disease, even under the most unfavorable conditions.<sup>13, 14</sup>

From a tabulation of some of the recent reports, the mortalities in sulfonamide-treated cases of meningococcal meningitis, based on groups of from 200 to over 1000 cases, are estimated as follows: with sulfanilamide alone, 14 per cent; with sulfanilamide and antiserum, 25 per cent; with sulfapyridine alone, 8 per cent; and with sulfapyridine in addition to antiserum, 12 per cent. Only small numbers of cases treated with sulfathiazole have been reported to date,<sup>15-17</sup> but the results in these cases seem to compare favorably with those obtained with sulfapyridine. In view of the low concentrations of sulfathiazole that are obtained in the cerebrospinal fluid during treatment,<sup>18, 19</sup> it would seem either that this drug is highly effective in low concentrations or that the level of the drug in the cerebrospinal fluid is not by itself of particular consequence. At any rate, so far as meningococcal meningitis is concerned, the warnings against the use of sulfathiazole based on this factor do not now seem to be justified. Sulfadiazine has also proved to be as effective as any of the other drugs in the few cases in which it has been used.<sup>10</sup> Since, when properly used, sulfadiazine appears to be less toxic than the other accepted sulfonamides, it may prove to be the drug of choice in the treatment of meningococcal infections.

**Serotherapy.** The difficulties in evaluating the results of serotherapy alone in cerebrospinal fever have been pointed out in a previous progress report.<sup>20</sup> To determine with scientific precision whether, in actual practice, antiserum is of value as a supplement to sulfonamide therapy is almost impossible. This is obvious from a study of the data on which the mortality figures mentioned above are based, and also from a consideration of the difficulties involved in the use of serums. Combined therapy is usually reserved for the severest cases, or else antiserum is given as a supplement to the sulfonamides in individual cases only after it begins to appear that the sulfonamides alone have failed to effect the desired cure.

Banks<sup>21</sup> has been sufficiently impressed with the results that he has obtained with chemotherapy alone to take the view that serum therapy is now unnecessary even as an adjuvant to chemotherapy. Other results from Britain suggest, however, that the mortality under chemotherapy is still over 20 per cent.<sup>22, 23</sup> The accuracy of these figures is, of course, open to question. Experimentally, the combination of sulfonamide and antiserum is more effective in curing meningococcal infections in animals than either agent alone.<sup>24</sup> Until more convincing data become available, therefore, it seems appropriate to reserve the immediate use of antiserum as a supplement to chemotherapy for the very severe or the apparently fulminating cases. It is particularly recommended for patients in coma in whom bacteremia is suspected. In other cases, antiserum need be employed only when there is no definite objective evidence of marked improvement after twenty-four to forty-eight hours of adequate chemotherapy. In any event, the serum used should contain antibodies specific for the infecting strain, and should be given intravenously in large doses with the usual precautions. Intrathecal administration should probably be avoided, at least until one is convinced that the disease is not being controlled adequately with drugs and intravenous antiserum.

The relative merits of antitoxin and antibacterial serum are still undecided. Hoyne<sup>25, 26</sup> advocates the use of antitoxin, although experimentally it appears to show no properties other than those due to the antibacterial immune bodies that it contains.<sup>27-29</sup>

Certain details concerning therapeutic procedures and diagnostic methods will be considered later.

### *Streptococcal Meningitis*

The mortality in cases of streptococcal meningitis has been reduced from over 95 per cent to less than 35 per cent by the use of sulfonamide

drugs<sup>30-33</sup> Sulfanilamide was the first drug to be used in this disease and, since it has proved highly effective, is still preferred by most physicians. Sulfapyridine is probably more effective, and successes with it have been reported. The use of other sulfonamides has not been reported in sufficient numbers of cases to warrant any opinions. Sulfathiazole should probably not be used because it is less effective against the streptococcus, in addition to the fact that high levels of this drug are difficult to maintain even in the blood. Sulfadiazine has proved to be highly effective in some other streptococcal infections<sup>34</sup> and will probably become the drug of choice, but data concerning its use in meningitis are not yet available.

Recoveries under sulfonamide therapy have been reported not only in meningitis caused by beta-hemolytic streptococci, but also in cases due to *Streptococcus viridans*<sup>35-37</sup> and even in isolated cases due to anaerobic streptococci.<sup>38</sup>

Antistreptococcus serums are probably of little or no value. Scarlet-fever antitoxins or convalescent serums, however, have been employed in some cases of postscarlatinal or other streptococcal meningitides. Apparently beneficial results have been reported from their use either alone or as a supplement to chemotherapy.<sup>39-40</sup> They are probably best reserved for patients with severe toxemia, especially when a rash is present.

### *Pneumococcal Meningitis*

There can be little doubt that almost all the numerous cases of recovery from pneumococcal meningitis that have appeared in the literature during the past four years are attributable directly to the use of sulfonamide drugs, since only isolated patients were previously known to survive this disease. Several authors,<sup>41-46</sup> in reviewing the recent literature, have estimated the mortality in sulfonamide treated cases to be about 35 per cent. This seems to us to be a deceptively low figure, since the great majority of failures remain unreported. Our recent experience suggests that the gross mortality in unselected cases receiving sulfonamide therapy, with or without other measures, is more nearly 80 per cent. Recoveries, however, have been reported in very severe and bacteremic cases,<sup>47</sup> in infants,<sup>48-50</sup> and even when the disease is complicated by cavernous sinus thrombosis.<sup>51</sup>

Specific antipneumococcus serums, alone or supplemented by various forms of drainage, may have been responsible for some recoveries prior to the introduction of sulfonamide therapy.<sup>42-52-54</sup> In experimental Type 1 pneumococcus meningitis in

rats, a greater percentage of recoveries may be obtained from the combination of specific antiserum and sulfanilamide than from either agent used separately.<sup>55</sup> This is difficult to demonstrate in human cases, although many of the recent reports of recoveries suggest that antiserum may have played a significant role when used to supplement chemotherapy.<sup>42-45-48-50-59</sup> The antiserums were given intravenously in all cases, but intrathecal injections, with or without complement, were used in some.

Sulfanilamide, which is known to have only relatively slight bacteriostatic action against the pneumococcus, has apparently been solely responsible for a number of the reported recoveries.<sup>46, 60</sup> It is our belief that in such cases the immunologic conditions were favorable, or that the organisms were highly susceptible or that both these factors were operative. Finland and his co-workers,<sup>53</sup> just before the introduction of sulfapyridine, reviewed the immunologic aspects of pneumococcal meningitis and outlined a therapeutic regime based on what was then known of the action of sulfanilamide and on the supposed mechanism of recovery in sulfanilamide treated cases. This regime included intensive treatment with sulfanilamide supplemented by intravenous antiserum and the intrathecal injection of antibodies and complement. It was realized that the administration of antibody probably was not essential in all cases and that, in practice, the intrathecal treatments would be necessary only in selected cases. It was to be expected, of course, that the introduction of more powerful antipneumococcus sulfonamides would reduce the necessity for serum therapy in many cases. Indeed, recent experience has indicated that a high percentage of recoveries may be expected from chemotherapy alone if intensive treatment with such drugs is undertaken from the beginning. Thus, the intravenous use of sodium sulfapyridine to initiate treatment and to maintain high blood concentrations during the first one or two days of therapy was probably responsible for the large proportion of recoveries in some of the recent reports.<sup>47, 61</sup>

Data on the uses of sulfathiazole and sulfadiazine in pneumococcal meningitis are scant, and judgment concerning the value of these drugs must therefore be reserved. Sulfadiazine seems to be advantageous, since it is effective in other pneumococcal infections and higher levels can be maintained with relatively fewer toxic effects when it is properly used.

Ross<sup>62</sup> reported a case of pneumococcal meningitis in which "drug resistance" was apparently acquired in the course of two or three days

of treatment with sulfapyridine. This occurrence is probably quite rare. Schmidt and Sesler<sup>63</sup> have recently shown that pneumococci that have become resistant to sulfapyridine are just as susceptible to hydroxyethylapocupreine as the parent strains. Since it has been shown that pneumococci which have become resistant to one effective sulfonamide are equally resistant to others,<sup>64, 65</sup> it may be necessary to resort to hydroxyethylapocupreine in cases in which sulfonamide fastness can be proved.

### *Influenza-Bacillus Meningitis*

The gross mortality in untreated cases of this disease is over 90 per cent, and the most vital single prognostic factor is the age of the patient. Almost all infants less than two years of age succumb.<sup>66</sup> Of the six known types of *Haemophilus influenzae*, Type B produces the great majority of the meningeal infections in infants and children. Most of those in older patients are probably due to other types or to the rough strains normally found in the respiratory tract. It seems likely that many of the spontaneous recoveries and the recent successes with chemotherapy alone occurred in patients infected with these rough or respiratory strains. There is, of course, no relation between influenza-bacillus meningitis and epidemic influenza, the latter now being known to be due to a specific virus.

Although there are a number of reports of recoveries from sulfonamide drugs alone, most of these occurred in the older age groups. The sum total of the results, although encouraging, is not very striking.<sup>56</sup> Many observers failed to obtain any favorable results with the use of drugs only, and that has been our experience. Final judgment on the effectiveness of sulfonamides alone, however, awaits more extensive data.

During the past few years, specific antiserum prepared in horses has been used intravenously and intrathecally, both with and without complement, in the treatment of meningitis due to the Type B influenza bacillus. Although the gross mortality may have been reduced to about 80 per cent,<sup>67</sup> the results in general have been far from satisfactory. More recently, however, rabbit antiserum specific for Type B has been used with encouraging results.<sup>68, 69</sup> Most of the patients treated with rabbit antiserum received chemotherapy in addition, and the role of each of these agents is thus difficult to evaluate. Davies<sup>69</sup> has treated a few patients with rabbit antiserum alone, and his results seem to indicate that this single agent may be as effective as the combined therapy.

The treatment recently outlined by Alexander<sup>56</sup> is as follows: sulfanilamide should be administered

immediately; fluids should be forced for three hours; and the equivalent of 25 mg. of antibody nitrogen intrathecally and 50 to 75 mg. of antibody nitrogen in a slow intravenous drip diluted in physiologic saline, Ringer's or sulfanilamide solution, should be given. The object is to neutralize all the free antigen and to establish and maintain an excess of antibody in the blood and cerebrospinal fluid. Such an excess is present when the serum gives rise to capsular swelling with the homologous organisms, or when the skin reaction to the specific polysaccharide is positive.<sup>70</sup> It is not certain whether the intrathecal treatment is essential. Information concerning the relative merits of the various sulfonamides is also lacking.

### *Staphylococcal and Other Bacterial Meningitides*

Recoveries from staphylococcal meningitis have been reported from the use of sulfanilamide,<sup>71, 72</sup> but successes have been more frequent with the use of sulfathiazole.<sup>73-77</sup> There have been 2 recoveries with sulfathiazole treatment at the Boston City Hospital. Sulfadiazine may also be useful in this condition, since it is highly effective against the staphylococcus.<sup>34</sup> Lyons<sup>78</sup> reported 2 cases of bacteremic cavernous-sinus thrombophlebitis treated successfully with a combination of sulfathiazole and heparin. One of these patients had clinical signs of meningitis that were confirmed by lumbar puncture.

Isolated cases of meningitis due to a large variety of other bacteria have been treated successfully with various sulfonamide drugs. These have included, among others, infections with colon bacilli,<sup>79</sup> Salmonella organisms,<sup>80</sup> Friedländer's bacillus,<sup>81</sup> gonococcus<sup>82</sup> and *Micrococcus tetragenus*.<sup>83-85</sup> Various sulfonamides have been used in these cases, either singly or in succession.

### DIAGNOSIS

The final etiologic diagnosis in any case of meningitis must be made on the basis of isolation or immunologic identification of the organism. The recent use of certain laboratory technics, mentioned below, permits an immediate final diagnosis in some cases. With the pneumococcus, for example, final diagnosis of both the organism and its type may be made merely from a stained smear and from capsular swelling with rabbit typing serum.

Clinical differentiation of the various etiologic types of meningitis is usually not possible. Certain general statements, however, may be made. During an epidemic of cerebrospinal fever, if evidences of purulent meningitis are present, the most probable etiologic agent is the meningococ-



cus, and the patient should be so treated, even though organisms are not found. Meningitis associated with otitis or mastoiditis is most probably due either to the pneumococcus or to the streptococcus. When an upper respiratory infection precedes meningeal involvement, the likeliest organisms are the pneumococcus, the streptococcus and, in children, the influenza bacillus. If furuncles are present on the face or elsewhere, staphylococcal infection is probable. It should be remembered that in infants and young children the influenza bacillus is being recognized as one of the most frequent causes of meningitis.

Although primary meningitis is usually due to a single organism, mixed infections may occur. These may be either simultaneous or consecutive infections. Such mixed infections are rare and, when they occur, usually follow primary infections outside the central nervous system.

The etiologic diagnosis is made in the usual way by cultures of the cerebrospinal fluid, the blood and pus from focal infections. Several recent techniques have facilitated an early diagnosis. The capsular swelling reaction may be carried out directly on the spinal fluid, on its sediment or on the initial culture after the morphology and staining characteristics have been determined by the methylene blue and Gram's stains. This method is of particular value with the pneumococcus, influenza bacillus<sup>50</sup> and Type 1 meningococcus.<sup>57</sup> The technique is similar in all respects to that employed in typing pneumococci in sputum. The precipitin test, employing specific antiserum and the clear supernatant spinal fluid, may be of value. This procedure may be used not only for etiologic identification of the causative organism, but also for typing the pneumococcus and the influenza bacillus. The test has also been employed in meningococcal infections, but in these direct typing may be complicated by the presence of the group-specific C substance.<sup>58</sup> In some patients, the infecting organism may be obtained from cultures of the nasopharynx early in the disease. The meningococcus is almost always found there in cases of cerebrospinal fever.<sup>59</sup> Mueller and Hinton<sup>60</sup> have recently described a simplified medium for the cultivation of the meningococcus. This medium has proved satisfactory for the primary isolation of gonococci and meningococci.<sup>10</sup> The growth of meningococci is facilitated by increased tension of carbon dioxide, which may be accomplished simply by the use of a candle jar.<sup>91</sup>

#### FOCAL INFECTIONS

The elimination of focal infections is of the utmost importance because of the tendency of men-

ingeal infections to become refractory to therapy if such foci are not removed. If the focus is apparent and if the local reaction is sufficiently advanced, immediate operation should be carried out for the relief of pressure and evacuation of pus. Often, however, it is difficult to localize the focus. In a recent article, Keefer<sup>7</sup> has indicated a number of signs that aid in the differential diagnosis. In general, chemotherapy should be instituted for twelve to twenty-four hours before operative procedures are undertaken, and should be continued for several days thereafter. The extent of the operation should be sufficient to eliminate nonvital tissue, particularly necrotic bone. Cultures should be made from all purulent foci at the time of operation.

#### LUMBAR PUNCTURE

The present tendency among some clinicians who are treating patients with meningitis is to avoid doing lumbar punctures, even to the extent of eliminating the procedure completely. This is an extreme view that is probably not justified. First of all, an initial lumbar puncture is necessary to establish the diagnosis of meningitis and to determine the etiologic agent. This is still extremely valuable to ensure the choice of the most effective drug and of the specific serum. With the usual precautions, the procedure does not jeopardize life or interfere with the subsequent recovery of the patient. In a recent review, Pray<sup>62</sup> found that lumbar puncture is not a significant factor in inducing meningitis, even in bacteremic patients. His data suggest that there may be a greater risk to the patient through failure to recognize the presence of meningitis if this procedure is not carried out. The first spinal fluid should be collected aseptically in separate tubes for culture and for chemical determinations. Estimation of the glucose content is the most valuable of the chemical determinations, since a low level is consistently found in bacterial infections. Total and differential cell counts should also be carried out, since they are of aid in distinguishing bacterial infections from those due to other agents. Thus, in tuberculosis, syphilis and the virus diseases (lymphocytic choriomeningitis, equine encephalomyelitis, St. Louis encephalitis and so forth), mononuclear cells predominate. In the course of differential counts, typical organisms are sometimes recognized in torula infections.

Lumbar puncture should be repeated for specific indications: for relief of the signs and symptoms of increased cranial pressure; to determine the progress of the case; to establish cure; for the diagnosis of relapse or recurrence; and for intra-

thecal therapy with antiserum when other methods of therapy fail.

### CHOICE OF SULFONAMIDE DRUGS

It should be clear from what has already been said that all patients with acute bacterial meningitis should receive sulfonamide therapy, but no hard and fast rule can be set down regarding the choice of drugs or the indications for specific serums and for other measures. The number of adequately studied cases is too small to warrant definite opinions. This is particularly true of the use of sulfadiazine in all kinds of meningitis and of all the drugs in infections due to influenza bacillus and the less common organisms. With these reservations, the following is our own tentative order of preference of sulfonamide drugs for various kinds of acute bacterial meningitis:

CAUSATIVE ORGANISMS	ORDER OF CHOICE			
	SULFADIAZINE	SULFATHIAZOLE	SULFAPYRIDINE	SULFANILAMIDE
Meningococcus	1	3	2	4
Streptococcus	1	4	2	3
Pneumococcus	1	3	2	4
Influenza bacillus	?	?	?	?
Staphylococcus	1	2	3	4
Gram-negative bacilli	1	2	3	4
Other pyogenic organisms	1	2	3	4

### INDICATIONS FOR THE USE OF SPECIFIC ANTISERUMS

Regarding the use of specific antisera as a supplement to chemotherapy, there is considerable disagreement among competent authorities. In our opinion, much depends on the particular conditions presented in each case. The following factors must be considered: the availability of potent specific antiserum against the infecting strain; the severity of the disease—severe cases may proceed so rapidly to a fatal outcome that one cannot afford to temporize, and it is probably better to be wasteful of serum than to regret having missed the opportunity to use it; the response of the patient to adequate doses of sulfonamides; when foci of infection prevent an adequate response to drugs, specific serums are useful, not in preference to removal of these foci but as an additional measure.

With these factors in mind, we now believe that the following recommendations are justifiable. Antimeningococcus serums should be given to patients with Type 1 infections as soon as the etiologic diagnosis is made only when the disease appears to be severe or fulminating. In other cases, such serums may be used if the infection fails to respond to adequate chemotherapy within twenty-four to forty-eight hours. A favorable response is indicated by the disappearance of fever, the failure to recover organisms from the cerebrospinal fluid and the return of the level of

sugar in the cerebrospinal fluid to normal. In meningitis due to pneumococci of known types, homologous specific rabbit antisera should be used under the same conditions. All patients with Type B influenza bacillus meningitis should receive specific rabbit antiserum as soon as the organism is identified. Scarlet-fever antitoxins or convalescent serums may be used in severe and toxic streptococcal meningitis, particularly if it is associated with a rash or if it occurs in the course of scarlet fever or as a complication of that disease.

### DOSAGE AND ROUTE OF ADMINISTRATION OF DRUGS AND ANTISERUMS

The recent trend in the dosage of sulfonamide drugs is to give large amounts during the early stage of treatment, to try to maintain as high a level as is consistent with safety and comfort until the infection is well under control, to give fairly large amounts of fluids (3000 to 4000 cc. a day) and to continue drug treatment in the same or in slightly reduced doses for fairly long periods, to ensure against relapses.

The intravenous use of 0.8 per cent sulfanilamide in physiologic saline solution or of a 5 per cent solution of the sodium salts of the other common sulfonamides in distilled water is usually recommended. It is used for the initial dose and for the first twenty-four to forty-eight hours of treatment in all patients and also later in those who vomit excessively or fail to maintain adequate blood levels. We have preferred to use the sodium salts of the sulfanilamide derivatives dissolved in physiologic saline solution—1 to 2 per cent for intravenous use (larger concentrations precipitate out at room temperature) and 0.5 to 0.7 per cent for subcutaneous injections. The latter route is preferred for all but the initial injection when parenteral therapy is desired, and, in our experience, this produces no local reactions. The daily dosage is 6 to 9 gm., depending on the weight, for each of the drugs. This total amount is given as the initial intravenous injection, and a similar amount is given daily in three equal portions at eight-hour intervals for sulfanilamide, sulfapyridine and sulfathiazole, and in two equal parts every twelve hours when sulfadiazine is used. Oral administration is used as soon as the condition of the patient permits, and the daily dose is then given in six equal parts at four-hour intervals. Treatment is usually continued after complete clinical and bacteriologic evidence of recovery for two to five days in meningococcal infections, for ten to fourteen days in pneumococcal and streptococcal cases, and for two to three weeks in all other cases.

Intrathecal injections of sulfanilamide or of sodium sulfapyridine are still recommended by some authorities, but most of them caution against the use of sulfonamides by this route. There is some evidence from the recent results in sulfithiazole-treated cases to suggest that the concentration of drug in the spinal fluid may not be of significance per se, although this point is not yet proved.

When specific serums are used, they should be given intravenously (or intramuscularly, if necessary). The amount should be such as to establish and maintain an excess of antibody in the circulating blood. This may be demonstrated in infections due to pneumococci and influenza bacilli by capsular swelling of the patient's organism in his serum or by the immediate positive skin test with the homologous type specific polysaccharide.<sup>70</sup>

Intrathecal injections of serum are probably not necessary in most cases, and some experienced physicians now advise against their use under any circumstances. We believe that the intrathecal use of antiserum should be reserved for patients who fail to respond favorably to adequate chemotherapy and intravenous serotherapy, thirty-six to forty-eight hours being allowed to elapse after adequate intravenous therapy. The advisability of the additional use of complement (fresh human serum) with intrathecal antiserum seems to be very debatable at present. In pneumococcal meningitis in adults, both antibody and complement may be given intrathecally in the least irritating form by using fresh serum obtained from the patient after a sufficient excess of antibody has been established by intravenous therapy.<sup>71</sup>

### COMPLICATIONS

Complications of meningitis have been remarkably rare in patients who have recovered following sulfonamide therapy. Deafness is still the most frequent complication in the cases of cerebrospinal fever and has also been observed in patients recovering from pneumococcal meningitis. Hydrocephalus is also seen in infants recovering from all kinds of meningitis. Relapses are not infrequent. The diagnosis and treatment of the relapse are essentially the same as those of the original infection.

### PROPHYLAXIS

For the prevention of epidemics of cerebrospinal fever in military forces, Mink<sup>93</sup> and Zinsser<sup>94</sup> have proposed gradual mobilization and "hardening" of new recruits. Lybourn<sup>95, 96</sup> advocates the search for and isolation of chronic meningococcal

carriers. Treatment of carriers with antiseptic sprays<sup>90, 97</sup> has been attempted, but the results are not conclusive. Sulfonamide drugs have been tried recently with some encouraging results<sup>98, 99</sup> Penicillin as a snuff<sup>100</sup> and tyrothricin as a spray<sup>101</sup> are now receiving a trial for the eradication of carriers.

The prevention of pneumococcal and streptococcal meningitis depends on the care of foci of infection and of injuries in and about the head. The use of sulfonamide drugs is recommended in the treatment of otitis and mastoiditis and also during and after all operations in which the cranial cavity is or may be entered.

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CASE RECORDS OF THE  
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., Editor

## CASE 27471

## PRESENTATION OF CASE

A thirty-year-old man was admitted because of increasing difficulty in breathing.

The patient had been well until a month before entry, when there was sudden onset of cough, productive of purulent sputum. Nine days later, night sweats and chills appeared. When admitted to a sanatorium three days later, the patient was acutely ill and dyspneic, with rapid pulse and high fever. There was dullness throughout both lung fields, with a few medium rales in the left. On the fifteenth day of the illness, the blood showed a red-cell count of 4,950,000 with 85 per cent hemoglobin, and a white-cell count of 4400 with 79 per cent polymorphonuclears, 9 per cent lymphocytes, 11 per cent monocytes and 1 per cent basophils. A week later the white-cell count was 4500, and three days after that it rose to 6400 with 91 per cent polymorphonuclears. The sedimentation rate was 8 mm. The tuberculin test was negative up to 1 mg. The urine was essentially normal. Culture of the sputum showed mixed organisms, with staphylococci predominating; on another examination, a pure growth of hemolytic staphylococcus was isolated. Tubercle bacilli could not be found by concentration tests. Agglutination tests for typhoid and paratyphoid fevers, undulant fever and tularemia were negative. A course of sulfathiazole was given from the twentieth to the twenty-seventh day of the illness, and a blood level of 4 mg. per 100 cc. was attained. The drug was discontinued because of the appearance of a rash, and because of the absence of benefit. The patient continued acutely ill and febrile. His pulse ranged from 120 to 138, with respirations from 46 to 48. There was increasing cyanosis and dyspnea.

The past and family histories were not of significance.

On admission, the patient appeared thin and wasted. The skin and mucous membranes were quite cyanotic. The lips were covered with sordes, and the nostrils bore crusted hemorrhagic lesions. The trachea and heart were displaced to the left. Loud wet rales were heard over each upper-lung

field, with loud tubular breath sounds, and resonance was preserved in these areas. There were small moist rales in the lower two thirds of the right chest, with absence of breath sounds and with percussion dullness. A pleural friction rub was heard at the left base. The heart sounds were obscured by the lung noises. The abdomen was slightly tympanitic. Rectal examination was negative. There was well-defined pitting edema of both legs. The calves were soft, cool and free from tenderness.

The temperature was 102°F., the pulse 138, and the respirations 50. The blood pressure was 120 systolic, 75 diastolic.

Examination of the blood showed a white-cell count of 15,000 with 80 per cent polymorphonuclears. The red-cell count was essentially as noted in the other hospital. The nonprotein nitrogen of the blood was 23 mg. and the total protein 4.5 mg. per 100 cc.; the chlorides were 88 milliequiv. per liter. The van den Bergh reaction was 2.4 mg. per 100 cc., biphasic. The urine showed + tests for albumin, diacetic acid and bile. The sediment contained occasional white cells. The sputum grew *Staphylococcus aureus*.

A roentgenogram of the chest showed a large amount of fluid in the right pleural cavity, obscuring the right diaphragm and costophrenic angle, and extending upward in the axillary line as far as the apex. Dense consolidation radiated from the hilus on each side. The left pleural cavity seemed free of fluid. There was no evidence of cavitation.

A right thoracentesis yielded 1320 cc. of thin, free-flowing, yellow, slightly turbid fluid from which *Staph. aureus* was grown. The patient's respirations at once became less labored, and his color improved, changing from blue to pink. He was given oxygen, however, and started on sulfadiazine. Several hours later, he became irrational, and required restraint. The next day, trocar thoracotomy was performed, with drainage of about 600 cc. of fluid in twenty-four hours. The patient seemed improved. A blood transfusion was given and was repeated on the fourth hospital day. At this time, there was much emphysema of the subcutaneous tissues about the trocar wound. The edema of the legs extended as high as the sacrum. The urinary output for the day was only 330 cc., with a specific gravity of 1.032 and with a ++ test for albumin. It was thought that the concentration was related to the therapy, since a sulfadiazine blood level of 10.8 mg. per 100 cc. had been attained. At this time, a roentgenogram of the chest showed numerous hazy areas of in-

creased density in the portion of the right lung that had previously been obscured by fluid.

On the sixth hospital day, a firm, slightly tender mass was palpated in the splenic area, extending two to three fingerbreadths below the costal margin, and descending with respiration. Two days later, this mass reached four fingerbreadths below the costal margin. The liver edge was not palpable. Repeated transfusions were given. The patient remained comfortable as long as he was kept in an oxygen tent. On the eighth hospital day, the temperature began to spike from 99 to 104°F. Late on the tenth day, he again became increasingly dyspneic and cyanotic. The respirations fluctuated from 50 to 60, and the pulse from 150 to 160. There was an increase in moist rales throughout both lung fields, without extension of the mediastinal shift. Tourniquets to the extremities gave no apparent relief. The patient became irrational and unmanageable. On the twelfth and last hospital day, he was quite unresponsive. After an apparent brief convulsion, he was found to have a stiff neck. The head was fixed toward the left. There was cogwheel rigidity of muscles. The eyes were held open, and the pupils were unequal, reacting sluggishly. The fundi were normal. A lumbar puncture gave clear fluid, under an initial pressure of 100 mm. of water. The fluid contained 2 or 3 lymphocytes per cubic millimeter. In the last hours, the right pupil dilated and became fixed. There were choreiform movements of the arms and legs. Respirations gradually ceased.

#### DIFFERENTIAL DIAGNOSIS

DR. WILLIAM B. BREED: I should like, first of all, to simplify this story and follow it through more or less as a straightforward acute upper respiratory infection, with purulent staphylococcal bronchopulmonary infection; and I think we can do that, particularly if we take at face value the sudden onset of disease one month prior to entry.

Apparently, the patient had an acute upper respiratory infection, with sudden onset, which progressed; he probably developed a bronchial fistula, with empyema due to *Staphylococcus aureus*. Because of this illness, he did develop some avitaminosis. The serum protein was low, perhaps because of a nutritional factor.

Certain things about this story, if one reads it over a number of times, need explaining. The first is the leukopenia found in another hospital; another is the x-ray picture, which I am not clear about and which I want cleared up. Still another is the appearance of a mass under the left costal margin in the region of the spleen, which I think

we must accept as an enlarged spleen. Moreover, involvement of the central nervous system cannot be explained on the basis of acute fulminating bronchopulmonary infection alone. Before coming here, I asked one of our hematologists if, from the record, he could say that this leukopenia, which is reported with 11 per cent monocytes and a high polymorphonuclear count, indicated some underlying blood dyscrasia, such as lymphoma or aleukemic leukemia. He replied that it could represent such a condition, but that no such diagnosis could be made from the blood report alone. I agreed with that. However, I do think that we must consider the initial leukopenia with a monocytic increase as possibly being important in the fundamental diagnosis.

Now I should like to get more information on the x-ray findings.

DR. AUBREY O. HAMPTON: I am afraid I am not going to give you as much information as you would like. Almost any radiologist who saw these films would first think of pulmonary edema, because any type of pneumonia that would advance to that degree is seen only post mortem. I do not believe that a patient with pneumonia, other than tuberculous pneumonia, of that extent could still be alive, particularly for so many days.

DR. DONALD S. KING: The films taken in the sanatorium two weeks previously looked like that.

DR. BREED: Did you see them?

DR. KING: Yes.

DR. HAMPTON: I cannot be sure that there are abscesses in the lungs. Pulmonary edema, I think, should be ruled out because it did not change enough in the whole period of ten days. The most definite change occurred when they drained the fluid in the pleural cavity.

DR. BREED: Do you think that the patient had pleural sepsis with bronchial fistula?

DR. HAMPTON: The pleural fluid was not true pus, was it?

DR. CHAMP LYONS: It was a thin fluid, which on culture gave a heavy growth of *Staph. aureus*.

DR. HAMPTON: I should not expect it to have been real pus, because when it was drained the lung promptly expanded.

DR. BREED: And there was no bronchial fistula?

DR. HAMPTON: I do not believe so. I do not see any enlarged lymph nodes. In one of the films, there is a gas bubble, probably very high in the splenic flexure. I doubt very much if the spleen was enlarged. I think one would have to call this chronic bilateral pneumonia, with fluid in the right pleural space.

DR. BREED: There are no multiple abscesses?

DR. HAMPTON: I cannot be sure. These small areas of diminished density are not clear enough for me to make a diagnosis. There is overlying air in the pleural cavity—it might be interspersed between adhesions or fibrin.

DR. BREED: It is very difficult to believe this man was entirely well a month before entry into the hospital.

DR. BREED: What was his occupation?

DR. TRACY B. MALLORY: He was a tube annealer.

DR. BREED: That does not help. I suppose a tube annealer is not a candidate for pneumoconiosis.

DR. HAMPTON: The diagnosis would have to be acute silicosis if the lesion were due to dust.

DR. BREED: I think it is obvious that this man was not completely in good health one month previous to entry, when he had a sudden onset of cough followed by nine days of sweats and chills; and I am therefore prepared to make a few conclusions about the underlying lesions. I can assure you, however, that it will be mostly guesswork because there is no accurate laboratory evidence.

DR. HAMPTON: I now have the film taken in the sanatorium a month before the one I previously demonstrated. The patient obviously had considerable pulmonary disease at that time. It started out as small and large rounded areas of density. There were some small miliary lesions.

DR. BREED: Could they be multiple staphylococcal abscesses?

DR. HAMPTON: I do not believe so.

DR. BREED: The sputum contained many staphylococci, and also the pleural fluid. Is it not so?

DR. HAMPTON: Yes.

DR. BREED: In any event, I am prepared to believe that the staphylococcal infection was not the primary cause of death. There was undoubtedly a superimposed bronchopulmonary infection due to the staphylococcus.

Nothing is stated about the cardiac situation; therefore, I must ignore it. The tourniquets put on the legs suggest some sort of cardiac failure, but I cannot be sure of that.

This question of the sudden appearance of the spleen interests me a great deal; I venture to suggest that it had been present for a long time, and that someone found it one morning.

DR. KING: It was noted in the sanatorium.

DR. BREED: I am glad to hear that because according to the record it appeared during the patient's stay in this hospital. Splens do not appear all of a sudden. Moreover, I question whether

its size really increased in two days. It certainly does not seem reasonable to believe that the spleen had increased in size in a few hours. Therefore I think this man had a chronic disease. On it was superimposed the infection that is here described.

What lead have we concerning the underlying process? If we place emphasis on the leukopenia and the spleen, we might very well consider one of the new growths of the lymphoid series, possibly lymphoma. Having thought of such a possibility, I recalled a case that was somewhat similar to this one in which during life the diagnosis was impossible, and in which the post-mortem examination showed nothing but a peribronchial infiltration by lymphomatous tissue. There were no lymph nodes, and I could never feel the spleen. Whether the patient in the case under discussion had lymphoma or aleukemic leukemia, I do not see how we can do more than guess but I do believe that he had an underlying disease a good while before the month previous to admission. The edema and the sordes and crusts on his nose are not very important except as they indicate a very sick man with malnutrition and riboflavin deficiency.

I have to conclude with the thought that the patient had a lymphoma, a lymphosarcoma or one of the lymphoid series of new growths, with, possibly, some peribronchial infiltration, and that the infection was entirely secondary. Of course, he died of the infection. He would have died of the underlying disease eventually, and it was responsible for the continuing and very bizarre pulmonary infection.

DR. KING: I think you went just far enough. You did a lot better than I thought anyone could possibly do. The patient was sent to the Middlesex County Sanatorium with the diagnosis of pulmonary tuberculosis. He ran a septic temperature, but we could find no evidence of tuberculosis. Many sputum examinations failed to show tubercle bacilli; however, the sputum did show a pure culture of *Staph. aureus*, and the blood culture showed one colony of staphylococcus. We sent the patient into this hospital, thinking that he had staphylococcal pneumonia and septicemia. After his admission here, a chest tap produced a fluid that showed staphylococcus on culture, and I believed that we were dealing with an overwhelming staphylococcal infection. But the course after that made it evident that we were dealing with some unusual condition. No one thought of lymphoma.

DR. BENJAMIN CASTLEMAN: How can you rule out carcinoma?

DR. BREED: I cannot; I forgot to mention the possibility of metastatic carcinoma, which I had considered and discarded because of the leukopenia and the splenomegaly.

DR. HAMPTON: Dr. Lingley and I have been looking at these films, and we agree that the x-ray picture at the first examination looks like that of metastatic neoplasm. I do not know the answer to this case. I noted that the first film was marked tuberculosis, and I erased it before Dr. Breed could see it. I am still going to have my say, however. Later on, the process becomes confluent, like infection, not like metastasis, and the only confluent tumor such as this that I know of is lymphoma. I am therefore inclined to agree with Dr. Breed, especially since Dr. King has complimented his diagnosis.

#### CLINICAL DIAGNOSES

Staphylococcal pneumonia.  
Multiple liver abscesses.

#### DR. BREED'S DIAGNOSES

Lymphoma (? peribronchial).  
Staphylococcal pneumonia, empyema and septicemia.

#### ANATOMICAL DIAGNOSES

Reticulum-cell sarcoma of lungs and kidney.  
Multiple pulmonary infarcts.  
Staphylococcal empyema.  
Septic spleen.  
Thrombophlebitis of femoral veins, bilateral.  
Operative wound: right thoracotomy.

#### PATHOLOGICAL DISCUSSION

DR. MALLORY: We were startled at autopsy by the appearance of the lungs. Both lungs were virtually filled with tumor nodules running from 0.5 to 1 cm. in size. Many showed central necrosis, sometimes with dimpling of the surface, such as one sees with carcinoma. However, they were soft and in that way unlike cancer. There was very little other evidence of tumor. There were a number of slightly enlarged lymph nodes along the aorta, which, however, were not clearly neoplastic. There was, of course, the remnant of staphylococcal empyema, with thick fibrinopurulent exudate in the pleural cavity. One single metastasis about 2.5 cm. in diameter was found in the kidney.

On microscopic examination, it was immediately obvious that this was a lymphomatous tumor, and I should classify it as a reticulum-cell sarcoma. There was not very much peribronchial infiltration, but there was a good deal of perivascular infiltration, with invasion, in many places,

of the arterial walls, and secondary thrombus formation.

So far as the peripheral edema of the legs was concerned, although the serum protein may have played a role, I think it was primarily due to thrombophlebitis of both femoral veins. The spleen was large but not involved by neoplasm. I should have to classify it as a septic spleen.

DR. HAMPTON: Was the intervening pulmonary tissue between the nodules normal?

DR. MALLORY: There was a great deal of tumor not all of which was limited to the sharply outlined nodules seen on gross examination. There was also vaguely outlined infarction; most of it was in tumor tissue, but some was not. This infarction, I think, was due largely to local thrombosis rather than to embolism dependent on direct invasion of the pulmonary arteries by tumor.

DR. HAMPTON: There was no edema?

DR. MALLORY: There was some, but not a great deal.

#### CASE 27472

#### PRESENTATION OF CASE

A fifty-eight-year-old housewife was admitted to the hospital for treatment of a fracture of her right thigh.

She had been seen in the hospital twelve times before, over a period of seven years, because of rheumatoid arthritis involving definitely the fingers, wrists, elbows, shoulders, feet and ankles, and involving questionably the knees, hips and spine. Following her twelfth hospital stay, her joints had appeared to improve, with some restoration of function. The only evidence of active disease was constant elevation of the sedimentation rate. The night preceding her final entry, she slipped from the edge of a bed on which she had been sitting, and fell to the floor, fracturing her right thigh above the knee.

On examination, the patient displayed the same hypertrophic changes of joints as had characterized her arthritis on earlier admissions, except for some progression of the disease in the right shoulder. There was a simple fracture of the right femur, above the knee. The heart, lungs and abdomen were essentially normal.

The temperature was 98°F., the pulse 108, and the respirations 20. The blood pressure was 140 systolic, 70 diastolic.

Examination of the blood at the time of the twelfth admission five months previously had shown a red-cell count of 4,880,000 with 16.1 gm. hemoglobin and a white-cell count of 11,400 with 74 per cent polymorphonuclears. The sedimen-



tation rate was 17 mm per minute Examination of the urine was negative

A roentgenogram of the right thigh showed a comminuted fracture of the lower end of the femur, about 25 cm above the condyles, with the fragments in excellent position

The fracture was treated at first by suspension with traction, and later by application of a plaster cast At the end of the seventh hospital week, the cast was removed and a splint applied to permit exercise A roentgenogram at this time showed a small amount of callus, the fracture lines still remaining distinct The patient received physiotherapy treatments, including the Hubbard tub, but continued to lack muscle strength After four months, active exercise was begun

A month later, in her thirty fifth week in the hospital, she spent a restless night and vomited without apparent cause The next day, she was incontinent of urine and remained in stupor from which she could be roused There was slight weakness of the left eyelid and left side of the face, and the tongue deviated slightly to the left The patient was able to move all her extremities, and there was no loss of sensation The tendon reflexes were hyperactive and equal The plantar responses were equivocal Speech was distinct, without aphasia or inco-ordination The temperature, pulse and respirations remained normal The blood pressure was 150 systolic 95 diastolic The next day, the patient was drowsy, but otherwise seemed normal

Nine days after the onset of this attack, the patient again became drowsy She had been complaining of frontal headache, "like the pressure of a telephone operator's headset" The next day, her stupor became deeper and she responded only to painful stimuli Her lips were cyanotic, her eyelids retracted, and the right eye deviated to the left The pupils were equal and responded to light The fundi appeared normal The deep reflexes were active and equal The plantar reflexes showed withdrawal reactions The right side of the face seemed more relaxed than the left There were no abnormal signs in the chest or abdomen The blood pressure was 150 systolic, 90 diastolic During the next four days, the temperature, pulse and respirations rose gradually, reaching terminal levels of 106.4°F, 160 and 48, respectively Death occurred at the end of the thirty seventh hospital week, following several right sided convulsive movements

#### DIFFERENTIAL DIAGNOSIS

DR MAURICE FREMONT-SMITH I approach this case without my usual confidence that I have a

chance of getting something right Perhaps some of the observations were not correct, certainly, there are very large gaps in the information given us I should like very much to throw the case open to interruptions from the floor,—especially since I see three neurologists sitting here,—because I am sure that I cannot make a very satisfactory discussion

In the first place, the patient was admitted without apparently much the matter with her, except that she had a great deal of some sort of arthritis She fractured her leg, was appropriately treated, and progressed satisfactorily for many weeks Then, one night, she developed restlessness, vomiting and, the next day, stupor and cranial nerve paralysis, she undoubtedly died from an intracerebral accident of some sort Is there very much to help us in making a diagnosis? The patient had rheumatoid arthritis—she had been in the hospital twelve times previously, and that had been the diagnosis On the other hand, we have the statement in the third paragraph that she displayed the same hypertrophic changes of the joints as had characterized her arthritis on earlier admissions That must be, I think, a misprint, or else she did have hypertrophic changes along with the underlying rheumatoid arthritis There was not very much to indicate that the rheumatoid arthritis was still active, except the sedimentation rate, which is good evidence It should be pointed out, however, that a sedimentation rate can sometimes get us off the track Dr J Burns Amberson, Jr, yesterday at the New England Postgraduate Assembly, pointed out the difficulty in recognizing tuberculosis in the age groups from fifteen to twenty two Tuberculosis can go on in a few weeks to rapid involvement of the whole lung and to death, and yet in the early stages there is no cough, no temperature, no rise of pulse and no increase in sedimentation rate—nothing except films that show the disease One cannot therefore eliminate active infection on the basis of a normal sedimentation rate There are, moreover, and I throw this open for discussion, some older people of sixty five or so who have high sedimentation rates—really high I have followed several of them for years, I do not know what is causing the high sedimentation rate, which occurs without anemia and without the development of any disease However, this patient had a high sedimentation rate, and we may accept the fact that she had active atrophic arthritis but I cannot see any connection myself between this and her death Perhaps there is a connection I shall be glad to have remarks from authorities

The only statement we have about the broken leg is that at the end of the seventh hospital week the x-ray films showed a small amount of callus and the fracture lines were distinct. I asked one of the surgical men what he would expect x-ray study to show at the end of the seventh week. He said that he would expect to see a little callus and a fracture line; consequently that is apparently normal healing of the bone. If the patient had had faulty union, one could speculate on the causes of delayed union. She had a fracture, and physiotherapy was given. The Hubbard tub, I am sure, is important, but I do not know why. Then exercises were begun, and a month later she had an episode. It seems to me that this episode, which undoubtedly was some sort of cerebral accident, was entirely independent of anything that had gone before. The patient was in the hospital and had a cerebral accident. That is all I can say. She did not have fat embolus, which comes at the time of fracture and causes collapse. That is out unless there is something abnormal about the fracture. Do we have the x-ray films?

DR. TRACY B. MALLORY: Unfortunately, they were lost.

DR. FREMONT-SMITH: I was sure of it. I knew it as I read the case. If it were a pathological fracture, and if union had been delayed, and it apparently was not, I could discuss with interest the possibility of metastasis, but so far as I can see that is bringing it in by the heels. There is no reason to do so, but there is no reason to bring in anything else either. There is no focus to give emboli, no hypertension. The patient had a good blood pressure for her age. She did not have nephritis, with the possibility of injury to the blood vessels. I should like to tie up the arthritis with her death, but I do not know of any reason to connect it with a vascular accident in any part of the body or brain.

DR. WALTER BAUER: If it is of any help to you, I might add that the patient was older than the stated age.

DR. FREMONT-SMITH: That does help a little bit. Something might have happened more easily.

DR. BAUER: That she had severe rheumatoid arthritis and marked secondary degenerative joints, which developed subsequently, there can be no doubt. She was bedridden when I first saw her and had about decided to remain so the rest of her life. It was only by persuasion and the help of a good strict nurse that she was finally able to walk with a cane and lead an independent life.

DR. FREMONT-SMITH: Although there is no evi-

dence for it, when I first saw the record I thought of coronary disease because it seems to me that there is a connection between rheumatoid arthritis and disease of the coronary arteries; but that does not help explain the cerebral accident. In a woman like this it is possible that emboli arose from a vein. But one would have to assume that the embolus went through the lung, or through a patent foramen ovale, either of which is improbable. We have no evidence. The heart was normal. There is nothing to help us. All we can do is discuss the various possibilities of a lesion that would cause such symptoms as these.

I thought first of metastatic disease—I do not know from where. I thought of vascular disease, and one can also pull some other things out of the air. One could think of marked hypoglycemia, which could cause coma and evidence of organic nerve changes, such as the Babinski reflex, but would not be fatal; there is no reason, however, to consider it. One can list brain tumor or brain abscess, but there is no reason to think of one more than another, except that the patient was old and vascular injury was more likely.

Granting that something happened, where did it happen? I pause specifically for help from the neurologists. How can a lesion cause coma and involve some of the cranial nerves—therefore, probably down around the area of the pons—without involving the pyramidal tract? They are careful to tell us that there was no hemiplegia. There is no information about Babinski signs except that they were equivocal. The patient had lesions that involved first one side and then the other. She probably had multiple basal lesions on the right, but how could they be in that region without involving the pyramidal tract? She did have a convulsion at the end, which theoretically suggests subcortical irritation, but any grave cerebral accident can result in convulsions. This convulsion, however, was right-sided. One would accordingly think of something in the left subcortical region. I have not spoken about subarachnoid hemorrhage, which I think is a possibility, although we are not told whether the neck was stiff. We have little information about the headache. Again, it is very hard for me to see why there was not more involvement of the nervous system if subarachnoid hemorrhage were present. I shall say, before closing the case, that if anyone does know it would be interesting to have more comment and more speculation on the neurologic situation.

DR. MALLORY: No lumbar puncture was done,

and that puts the neurologist at a great disadvantage.

DR. FREMONT-SMITH: No harder for him than for me!

DR. BAUER: There was a very good reason for not doing a lumbar puncture. This patient was between sixty-five and seventy years of age, rather than fifty-eight. We were quite certain that she was going to die. Furthermore, we knew that a post-mortem examination would be granted and that the cause of the cerebral symptoms would probably be ascertained at that time. Therefore, I did not think it necessary to do a lumbar puncture. Perhaps it should have been done for the benefit of this conference.

A PHYSICIAN: Would Dr. Fremont-Smith think of multiple lesions as a cause of the vagueness of signs?

DR. FREMONT-SMITH: I think that there must have been more than one lesion, and I should like a little comment from someone.

DR. MALLORY: Your preference is for a vascular lesion?

DR. FREMONT-SMITH: I should think so in a woman of this age.

DR. BAUER: What type of lesion?

DR. FREMONT-SMITH: I do not know.

DR. CHARLES S. KUBIK: There was drooping of the left upper eyelid. There was no difference in the size of the pupils.

DR. MALLORY: I should be inclined to vote against a vascular lesion. The patient had a very gradual deepening of symptoms, whereas most vascular lesions come on suddenly and then tend to improve. This showed the reverse.

DR. JAMES B. AYER: There is no explanation for the fever except on a neurologic basis?

DR. BAUER: No; not that we could find. It is only fair to say that the lungs were not examined posteriorly the last day or two.

DR. AYER: This case does not conform to vascular thrombosis; we lack the signs of bilateral cortical deficiency from thrombosis on both sides of the brain; and also we fail to have the findings of basilar-artery thrombosis.

Attention to the Hubbard tub is probably due to the fact that the hospital has recently acquired this useful article.

DR. BAUER: Since the patient had rheumatoid arthritis involving the right knee and a fracture of the right thigh, the treatment of which required a long period of immobilization, fibrous-tissue ankylosis occurred. I hated to think that this needed to be permanent. Therefore, she was treated in the Hubbard tub, in the hope that

we could prevent complete loss of motion of the right knee.

DR. MALLORY: Do you want to go ahead and tell us more about it?

DR. BAUER: We proceeded along much the same line of reasoning as Dr. Fremont-Smith did. Because of the sudden onset of headache, I first considered a subdural hematoma. As I saw the patient subsequently, I wondered if she might have multiple cerebral thromboses, a diagnosis that was not confirmed. I have forgotten what my final diagnosis was. I can assure you I was not certain of the exact cause of death.

A PHYSICIAN: Was the convulsion one sided?

DR. BAUER: I do not know. I did not see her at the time it occurred.

DR. MALLORY: The diagnosis was cerebral thrombosis.

## CLINICAL DIAGNOSIS

Cerebral thrombosis.

## DR. FREMONT-SMITH'S DIAGNOSIS

Cerebral lesions due to vascular injury.

## ANATOMICAL DIAGNOSES

Subdural hematoma, left, cerebral.

Rheumatoid arthritis, chronic.

Operative scars: left coracoid osteotomy; cholecystostomy; cholecystectomy; and appendectomy.

Fracture of right femur, old.

Peritonitis, healed, fibrous.

Pleuritis, healed apical, left.

Pulmonary edema, moderate.

Arteriosclerosis: coronary, moderate; aortic, minimal.

Leiomyoma uteri, with calcification.

## PATHOLOGICAL DISCUSSION

DR. MALLORY: At post-mortem examination, the significant findings were in the brain. There was, of course, generalized rheumatoid arthritis and a moderate amount of arteriosclerosis of the aorta and a slight amount of the coronary arteries, but nothing that should have functionally impaired the heart.

Dr. Kubik will tell us the interesting points in the brain.

DR. KUBIK: The finding of drooping of the left upper lid was probably significant. One might have expected an inequality of the pupils and dilatation of the left pupil as well. The lesion was a subdural hematoma on the left side, a fairly large one, surrounded by a rather thin membrane. It did not look as if it were old, and I should not

suppose that it resulted from the fall out of bed several months before death. I do not believe we have any indication of why this occurred. There was characteristic flattening of the frontal lobe by the hematoma, and slight displacement of the midline structures to the opposite side. There was actually some herniation of the medial surface of the hemisphere beneath the falx, a good deal of herniation of the cerebellum into the foramen magnum and slight herniation of the hippocampal gyri into the notch of the tentorium.

DR. FREMONT-SMITH: Should not the disks have been choked?

DR. KUBIK: They usually are not with subdural hematoma, and I should not expect them to be in a case of short duration.

DR. FREMONT-SMITH: Is not a spontaneous affair much more likely to be subarachnoid than subdural?

DR. KUBIK: Yes.

DR. BAUER: The patient had no stiffness of the neck. One would expect a higher temperature with a subarachnoid hemorrhage. These and other findings kept us from making this diagnosis.

DR. MALLORY: Can you see anything in retrospect that should have made one more suspicious of subdural hemorrhage?

DR. KUBIK: No; I do not.

DR. BAUER: After seeing the autopsy, I thought it was much more likely a spontaneous hemorrhage.

DR. KUBIK: I do not believe that it could have been due to the injury nine weeks before.

DR. BAUER: I think it is fair to say that the patient was not quite herself after the accident. She had nausea, vomiting and drowsiness, but there was no mention of headache.

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## ACCURATE BOOKKEEPING RECORDS OF HUMANITY

THE Bureau of the Census refers to the vital statistics of births and deaths as "accurate bookkeeping records of humanity," and the term is not overdramatized since on these data are based such figures as life-expectancy tables, population estimates, information on migration and fertility, and public health trends. The chief responsibility for accurate records rests on physicians, since 90 per cent of the births and deaths in the United States are attended by them. The officials charged with recording these data find it necessary each week to return many certificates, particularly those reporting deaths, because of the inaccuracy and vague phraseology employed.

A uniform vital statistics act was recommended

to the several states in 1939, but there is no guarantee that it will be adopted without change. Some form of registration procedure is required in every state, but the provisions vary to an amazing extent. Maine, in 1821, was the first state to pass legislation requiring registration, and Massachusetts followed in 1840; and complete records for births and deaths since 1848 are available in New Jersey.

The Department of Commerce, through the Bureau of the Census, publishes a pamphlet\* which contains the "International List of Causes of Death" and the additional information that every physician needs to know before he can execute a certificate correctly. Much of the confusion and discussion occurring in medicolegal situations could be decreased or eliminated if this or a similar reference were consulted and used. This is particularly true of those who are removed in point of time or distance from centers of medical education, the physicians in contact with hospitals and teaching services being more meticulous in their use of medical terminology.

The changing nature of our social concepts requires more frequent reference to birth and death certificates, and the physician has a dual obligation—to give more thought to the law and to his patient or the family, particularly to the latter. If he has familiarized himself with the case, he need not find difficulty in being specific. The certificate is of a confidential nature, and no physician should hesitate to indicate a disease such as chronic alcoholism if he is convinced that it is the principal cause of death. The contributory causes—those "which contribute to the risk of dying"—apply to minor underlying or accompanying conditions, including the use of alcohol and drugs. If there is doubt in the physician's mind about the actual role of any factor, a discussion of the case with the proper medicolegal officer may save much embarrassment and time for himself, the relatives and, in certain cases, the courts. If general terms must be used, they should be accompanied and linked with an

\*Physicians' Handbook on Birth and Death Registration. 94 pp. Washington: U. S. Government Printing Office, 1939. This can be obtained from the Superintendent of Documents, Washington, D. C., at a cost of 15 cents.

anatomic site. Medical terms which include the names of men should be avoided. Thus, exophthalmic goiter is preferable to Basedow's or Graves's disease.

The registration of vital statistics is maintained by city, state and federal agencies at considerable expense, and as a matter of economy alone, the basic material should be as carefully presented to the officials charged with registration as is a prescription to an apothecary.

## GRANTS FOR THE STUDY OF POLIOMYELITIS

THE National Foundation for Infantile Paralysis has awarded new grants totaling \$195,030 for research on the etiology, treatment and prevention of poliomyelitis, it was recently announced by Basil O'Connor, president of the foundation.

The objects of the foundation—the control and eventual eradication of the disease and the proper care of those afflicted—can be attained only by study of the virus, the exact nature of which is still unknown, of the most effective therapy and of the character and amelioration of the permanent consequences.

Of the twenty-eight grants made to achieve these purposes, three are of particular interest to physicians in Massachusetts. Two awards totaling \$6300 have been bestowed on the Children's Hospital in Boston to continue the study of the effects of infantile paralysis on the lower extremities and to inaugurate research to determine the effects of prolonged bed rest and other factors in the development of calculi or stones in the urinary tracts of patients with the disease. The Massachusetts General Hospital has received \$2500 to continue the study of clinical cases of infantile paralysis in which the patients have an unequal growth of the lower extremities. A study of the gastrointestinal tract as the portal of entry of the virus has been made possible by a grant of \$3000 to the Boston City Hospital.

The splendid work of the National Foundation for Infantile Paralysis merits the support of the medical profession and the laity. *The courage and*

zeal of the foundation in carrying on its relentless fight against a dreaded disease are an inspiration and a challenge to those who struggle against other diseases that threaten life and health.

## MEDICAL EPONYM

### LANE'S KINK

W. Arbuthnot Lane (b. 1856), surgeon to Guy's Hospital, London, first described this condition in an article, entitled "Chronic Constipation: A consideration of its surgical treatment," which appeared in *Surgery, Gynecology and Obstetrics* (6: 115-129, 1908).

... There can be no doubt that the pathological changes which are present in these conditions of imperfect drainage are most obvious and important. . . . The portion of the caecum above the brim of the pelvis, together with the ascending colon, is retained in a position of abnormal fixity to the posterior wall of the abdomen. This is affected [*sic*] by the development of adhesions between the outer aspect of the large bowel and the peritoneum covering the abdominal wall in its vicinity. . . . As a rule these adhesions merely fix the bowel, but occasionally they constrict its lumen very materially in one or more situations and render it liable to become obstructed. Not only do the adhesions anchor this part of the large bowel, but they also bind down to the iliac fossa a proportion of the appendix. . . . The result of this arrangement is that, when the caecum is loaded, it exerts a vertical strain upon the proximal portion of the appendix and causes that structure to become flexed abruptly at the lower limit of its adhesions. . . . When I recognise that the mechanics of the intestines have been altered to a degree that cannot be rectified satisfactorily by the division of bands, etc., I divide the ileum at a distance of about five or six inches from the caecum, . . . the descending colon and sigmoid are removed, the rectum . . . being occluded in the same manner as the ileum.

R. W. B.

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

#### SPONTANEOUS, INCOMPLETE ABORTION, FOLLOWED BY FATAL HEMORRHAGE

A twenty-eight-year-old para II was not seen until she was referred to the hospital by a physician who had been called by the patient because she was flowing.

The past history was irrelevant. Physical examination on admission was normal. The patient

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, Secretary, 330 Dartmouth Street, Boston.

was about three months pregnant, and was bleeding very freely. The pulse ranged from 120 to 140, and she was in some degree of shock.

The first step in treatment was a transfusion of 600 cc. of citrated blood. Then, the patient was examined vaginally. The placenta, which was found lying in the cervix, was removed, and the uterus packed. Since the patient continued to bleed, the pack was removed, and the uterus examined for retained pieces of tissue; none were found. In spite of the transfusion and stimulants, the patient died.

*Comment.* This is a case of spontaneous incomplete abortion associated with fatal hemorrhage. Massive hemorrhage from abortion is rarely seen before the twelfth week. Not infrequently, however, a patient with an incomplete abortion may start bleeding at six or eight weeks and continue to bleed freely off and on, which eventually results in a hemoglobin below 50 per cent and a correspondingly low red-cell count; such patients seldom bleed to the point of exsanguination.

Since it is reported that there were no products of conception left in the uterus in this case, the absence of contractility of the uterus must have been due to the lack of muscular tone that is associated with the shock that accompanies so many of these large hemorrhages. Everything possible seems to have been done for this patient. The record does not say that the patient had been bleeding off and on before the hemorrhage was alarming enough to cause her to seek medical advice. If this had occurred and if the patient had been under medical observation, with no attempt to investigate the cause of bleeding, the medical attendant might well have been criticized.

## DEATH

STOODLEY—HARRY M. STOODLEY, M.D., of Somerville, died November 5. He was in his sixty-fourth year. Born in Charlestown, Dr. Stoodley received his degree from Tufts College Medical School in 1904. He was a former member of the Massachusetts Medical Society. He is survived by his widow, two sons and a sister.

## CORRESPONDENCE

### NURSE-MIDWIVES

*To the Editor:* I was greatly interested in your editorial in the August 21 issue of the *Journal*, entitled "Maternal Welfare and the National Emergency," in which the use of the trained nurse-midwife in solving some of our problems of maternal care is suggested.

The Community Health Association, as you know, is the visiting nurse association for the City of Boston—a private agency dependent largely on the Greater Boston Community Fund for its support. In our nursing program, care of maternity patients is one of the biggest

services. Last year, for instance, over 8000 prenatal cases in the city were registered with us for nursing care and supervision. This includes care during the prenatal period, assisting the physician at the time of delivery if the mother is delivered at home, and care to mother and baby during the post-partum period. If the mother is delivered in the hospital, the nurse makes one or two visits after she returns home with her baby, to demonstrate the baby's bath and instruct the mother.

While the majority of maternity patients in Boston are delivered in hospitals at the present time, there are still a goodly number who remain at home under the care of a private physician or of one of the out-door delivery services conducted by the teaching hospitals. It is the policy of our association to give nursing supervision to prenatal cases only when they are registered with a physician or clinic, and we have always had excellent working relations with both private physicians and clinics.

In spite of this seemingly adequate maternity program in the City of Boston, we realize that there are still many maternity patients who go without prenatal supervision and only seek medical care when labor starts. Our nurses are constantly on the alert in their general nursing program to find these patients and to urge them to get under medical care. Even so, there are many that elude us.

Do you feel that there is a place in Boston for the nurse-midwife? Should we be urging some of our well-prepared nurses to secure this training and go into this field of service?

DOROTHY J. CARTER, *General Director*

Community Health Association  
Boston

\* \* \*

No one will deny that the care of maternity cases, particularly in Boston, owing in part to the efforts of the Community Health Association, has been markedly bettered in the last ten or fifteen years. The fact remains, however, as brought out in the editorial and acknowledged by Miss Carter, that many cases do not receive proper, if any, attention. Furthermore, in the event of mobilization, it is obvious that even more mothers would receive inadequate medical care. The editorial suggested that the possibility of utilizing, with rigid supervision, the trained nurse-midwife in crowded tenement districts and in sparsely settled rural communities—a practice now prohibited by Massachusetts statutes—be given due consideration. Ed.

### PREMARITAL MEDICAL EXAMINATIONS

*To the Editor:* The Massachusetts premarital health-examination law has been amended so that physicians on active service in the armed forces of the United States may make the required examination.

For this purpose the Department of Public Health has approved all serologic laboratories of the United States Army, Navy and Public Health Service and all laboratories operated by state health departments and by the District of Columbia. All other physicians practicing in Massachusetts must send the blood specimen for serologic examination for syphilis to an approved laboratory in Massachusetts.

A further amendment requires that the department furnish blank forms of certificates required under the act to city and town clerks.

PAUL J. JAKMAU, M.D.  
*Commissioner of Public Health*

State House  
Boston

## BOOK REVIEWS

*Biological Symposia*. Vol. I. *The Cell Theory; Mating Types and Their Interactions in the Ciliate Infusoria; Chromosome Structure*. Edited by Jaques Cattell. With a foreword by Albert F. Blakeslee, Ph.D. 4°, cloth, 238 pp., with 39 illustrations and 19 tables. Lancaster, Pennsylvania: The Jaques Cattell Press, 1940. \$2.50.

The Jaques Cattell Press is to be congratulated in making permanent the biological symposiums held at the Richmond meeting of the American Association for the Advancement of Science. These symposiums present the latest authoritative information in the various fields of biology. A good idea of the subject matter covered may best be obtained by listing the subjects discussed and the experts who participated in them.

The first symposium was on the cell theory; Dr. Joseph Mayer was chairman. The papers presented were: "The Cell Theory: Its past, present and future," by Dr. Joseph Mayer; "Microscopy before the Nineteenth Century," by Professor Lorange L. Woodruff; "Schleiden's Contribution to the Cell Theory," by Professor John S. Karling; "Predecessors of Schleiden and Schwann," by Professor Edwin G. Conklin; "A Modern Concept of the Cell as a Structural Unit," by Professor George A. Baitsell; "The Present Status of Mitosis," by Professor Franz Schrader; "The Problem of Cell Individuality in Development," by Professor Paul Weiss; "What of the Future?" by Professor Clarence E. McClung.

The second symposium was on mating types and their interactions in the ciliate infusoria; Dr. Herbert S. Jennings was chairman. After an introduction by Dr. Jennings, the topics considered were: "*Paramecium aurelia*," by Dr. Tracy M. Sonneborn; "*Paramecium bursaria*," by Dr. Jennings; "Studies on Conjugation in *Paramecium multimicronucleatum*," by Professor Arthur G. Giese; "Mating Types in *Paramecium caudatum*," by Lauren C. Gilman; "Mating Types in Euplates," by Richard F. Kimball.

The third symposium was on chromosome structure, with Professor Theophilus S. Painter as chairman. The topics considered were: "On Coiling in Chromosomes," by Dr. Bernhard R. Nebel; "The Physicochemical Nature of the Chromosome and the Gene," by Dr. C. H. Waddington; "The Structure of Salivary Gland Chromosomes," by Professor Painter; "Chromosome Structure as Viewed by a Geneticist," by Dr. Millislav Demerec.

*Biological Symposia*. Vol. II. *Speciation; Defense Mechanisms in Plants and Animals; Biological Basis of Social Problems; Regeneration*. Edited by Jaques Cattell. With a foreword by George A. Baitsell, Ph.D. 8°, cloth, 270 pp., with 13 illustrations and 1 table. Lancaster, Pennsylvania: The Jaques Cattell Press, 1941. \$2.50.

The second volume on biological symposiums will excite the interest of all students concerned with the phenomena of life.

The topics dealt with in the first symposium were: "Introduction," by Dr. Leon J. Cole; "Speciation of Fishes," by Dr. Carl L. Hubbs; "Ecologic and Genetic Variability within Species of *Peromyscus*," by Dr. Lee R. Dice; "Speciation from the Point of View of Genetics," by Dr. M. R. Irwin and Dr. R. W. Cumley; "Breeding Structures of Populations in Relation to Speciation," by Professor Sewall Wright; "Speciation Phenomena in Birds," by Dr. Ernst Mayr; "Speciation in *Peromyscus*," by Dr. Lee R. Dice; "Levels of Divergence in *Drosophila* Speciation," by Professor Warren P. Spencer; "Speciation

as a Stage in Evolutionary Divergence," by Professor Theodosius Dobzhansky.

The second symposium, on the topic of defense mechanisms in plants and animals, comprised: "Local Reactions in Plants," by Dr. Fritz W. Went; "Generalized Defense Reactions in Plants," by Dr. W. C. Price; "Local and Generalized Defense Reactions in Animals," by Dr. William Bloom.

The third symposium, on the biological basis of social problems, was composed of the following: "Introduction," by Dr. Samuel J. Holmes; "A Few Words About Nature," by Dr. William E. Ritter; "Social Integration as a Biological Process," by Professor Charles M. Child; "The Naturalist as a Social Phenomenon," by Dr. Francis B. Sumner; "The Ethics of Enmity in Social Evolution," by Professor Holmes; "A Biologist's Appreciation of Religion as a Factor in Social Evolution," by Dr. Edwin B. Copeland.

The fourth symposium, concerning regeneration, contained the following papers: "Introduction," by Professor J. William Buchanan; "The Histologic Basis of Regeneration and Reassociation in Lower Invertebrates," by Dr. Winterton C. Curtis; "The Environmental Control of Regeneration in Euplanaria," by Dr. Olin Rulon; "Aspects of Regeneration in Annelids," by Dr. Libbie H. Hyman; "Contributions to the Problem of Regeneration in Protozoa," by Dr. William Balamuth.

## NOTICES

## MASSACHUSETTS GENERAL HOSPITAL

A meeting of the Hospital Research Council will be held in the Bigelow Amphitheater of the White Building on Tuesday, November 25, at 5 p.m.

## PROGRAM

Effect of the Serum of Patients with Graves's Disease, Myxedema and Acromegaly on the Oxygen Consumption of Guinea-Pig Thyroid. Dr. Carlos Galli-Mainini.

Chemotherapy of Experimental Staphylococcal Infections. Dr. Champ Lyons.

Retardation of Epiphyseal Growth by Roentgen Irradiation. Drs. J. S. Barr, E. A. Gall and J. R. Lingley.

Further Studies on the Optimal Solution for the Dissolution of Calcium Phosphate Calculi. Drs. Fuller Albright, R. Murdoch, H. Suby and H. Sulka-witch.

## JEWISH MEMORIAL HOSPITAL

A diagnostic and therapeutic conference will be held at the Jewish Memorial Hospital on Thursday, November 27, at 11 a.m. Dr. J. H. Swartz will speak on "Diseases of the Skin."

Physicians and medical students are invited to attend.

## NEW ENGLAND PATHOLOGICAL SOCIETY

A meeting of the New England Pathological Society will be held at the Peter Bent Brigham Hospital on Thursday, November 27, at 8 p.m. Dr. William Dock, professor of pathology at Cornell University Medical College, will speak on "The Kidney and Hypertension."

Physicians and medical students are cordially invited.

(Continued on page xii)



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## MILITARY SYMPOSIUM

### FATIGUE IN AIRCRAFT PILOTS\*

Ross A. McFarland, Ph.D.†

BOSTON

ONE of the most significant problems in civil and military aviation relates to what is popularly known as "pilot fatigue." Conclusions about its nature or even its locus, however, are almost as numerous as the articles that have been written, since each depends largely on the interests or background of the author. Viteles<sup>1</sup> says that the word "fatigue" used both popularly and scientifically refers to three related phenomena: 'An over manifestation in the form of reduced output on the task known as work decrement, a physiological state involving changes in organic functions and the production of chemical products of fatigue, and a feeling of fatigue or tiredness.' Schneider<sup>2</sup> suggests that it 'is a progressive flagging of efficiency, together with subjective sensations of loss of control.' Grow<sup>3</sup> has advanced the hypothesis, based on wide experience in the field of aviation, that "fatigue is due to the excessive generation of nerve impulses and originates in the nervous tissue of the body."

The varieties of interpretation may be due in part to the fact that the word "fatigue" does not have a specific meaning in a scientific sense. It refers, generally speaking, to a related group of phenomena associated with loss of efficiency. In common usage, it is not unlike the word "unconscious" in psychopathology—a convenient category used to classify certain phenomena that are essentially unknown or not clearly understood, yet nonetheless real. The problem cannot be explained away, however, simply because agreement cannot be obtained relative to the phenomenon itself, its nature or its locus. In a practical sense, everyone, particularly a pilot after a long flight over difficult terrain and in adverse weather conditions, understands in a subjective

sense what is meant by the words "nervous and physical exhaustion" and "fatigue."

In this discussion, an attempt to be practical is made, since the flight surgeon is always faced with practical problems. An operations' manager or flight officer, for example, may approach him with such questions as these: The pilots on certain routine operations are returning to their bases completely exhausted, is the flying time too long? Do they fly at too high altitudes without oxygen? Or is there something in the cockpit that affects them adversely, such as vibration, noise or poor illumination? Or, again, Captain Jones does not seem to be himself these days. He has "gone stale." He is tense, nervous and irritable, and shows poor judgment in making decisions while in flight. He used to be one of the ablest pilots in the flight group, but his flying is no longer trusted. Should he be grounded or sent away on a vacation? Finally, in the daily press are recorded accidents attributed to "pilot error." In the early stages of the war, the British pilots were evidently losing more planes in landing accidents on returning home from fighting abroad than during actual combat with the enemy. In civil aviation in this country, a large percentage of the accidents (often estimated at 80 to 90 per cent) are ascribed to pilot error. Do these pilots become so exhausted that their judgment is faulty when they make decisions or land? Do latent or minor visual defects in acuity, in night vision, in space perception and in sensory motor performance become manifest or acute after long hours of fighting under intense emotional strain?

Since one cannot control and measure all the variables involved, the answers to such questions are indeed difficult. In a short discussion, one can hope to indicate only some of the more important contributing factors involved in pilot fatigue. Only brief mention is made, therefore, of the so-called "locus" of fatigue and of the accumulation of

\*This and the three subsequent papers were presented as part of a symposium at the annual meeting of the Massachusetts Medical Society, Boston, May 22, 1941.

†Assistant professor of industrial research, Harvard University; consultant Pan American Airways System.

fatigue substances. Emphasis is placed on the variations in energy resources, such as oxygen and sugar, and, more especially, on several major contributing factors to fatigue, such as worry, personal maladjustments, lack of exercise, the effects of high altitude, poor selection of food, the excessive use of alcohol and tobacco, and certain factors in the cockpit of an airplane, such as noise and vibration. Finally, a study of fatigue in transoceanic airmen is discussed.

### *Locus of Fatigue*

For many years, physiologists have attempted to locate fatigue in certain parts of the body—in the muscle itself, the nerve end plate, the nerve fiber, the synaptic junctions or the cortical cells of the brain. Numerous experiments have shown that the nerve fiber is almost indefatigable. These phenomena are demonstrated to students of physiology with the classic experiment involving a nerve-muscle preparation. A frog muscle, with its efferent nerves, is isolated; the nerve is stimulated until the muscle ceases to contract. Then, if the muscle is stimulated directly, it may react almost as vigorously as before. If the nerve is given a normal supply of oxygen and stimulated alone, it will continue to transmit impulses more or less indefinitely. By such procedures, attempts have been made to demonstrate the relative efficiency of the nerve and muscle and the possible location of fatigue in the nerve end plate or the synapses.<sup>4</sup> Although one can demonstrate that certain muscles are subject to loss of efficiency in ergographic studies, this sheds little light on the fatigue problem in aviation, in which the pilot's gross musculature is not used excessively. Studies of isolated nerve fibers have proved to be equally inconclusive concerning the basis of fatigue. Except for the role of oxidation in the efficient functioning of the nerve tissue, therefore, the implications of these experiments for pilot fatigue are not very direct.

It may be that the psychologists who have stressed the role of the higher cortical levels have more information to offer regarding pilot fatigue. They speak of mental "blocking," and they have demonstrated that, under certain conditions involving stress, there is a loss of efficiency in mental tasks.<sup>5</sup> This is especially true of the tasks that involve the more complex cortical functions, such as memory and delicate judgments of discrimination and choice.

In the field of vision, in which the processes involved are concerned essentially with minute muscle or nervous tissue, objective data on visual fatigue are very inadequate and inconclusive. Many

authorities believe that the frequency with which ocular defects are observed in children (often estimated at 40 per cent) and in adults is directly related to the various strains imposed on the eyes in modern life. Unfortunately, however, little is known about the basic causes of these abnormalities or of the contributing factors to visual discomfort or loss of efficiency in visual work. Even in an applied problem in industry, such as the amount of illumination necessary to prevent visual discomfort, one finds a wide divergence of opinion among equally prominent authorities. The problem is complicated by the nature of the visual mechanism itself—that is, the retina is an extremely complex organ, being essentially an extension of the brain. It involves only a small amount of tissue, it adapts itself readily to changes in the environmental setting, and it apparently recuperates rapidly from ordinary stresses. In fact, many believe that the retina is indefatigable. Experiments dealing with the ocular muscles used in reading show that they are not easily subject to a work decrement. Carmichael and Dearborn<sup>6</sup> have failed, for example, to find evidence of fatigue of the muscles of the eye during six hours of continuous reading. The records were made by attaching electrodes to each side of the eye so as to record the action potentials of the ocular muscles during reading. Although the basis of visual fatigue is not clearly understood, it is essential to protect the pilot from variables known to accentuate visual discomfort, such as excessive glare from the clouds or sun, reflections from metal surfaces on the plane and poor illumination in the cockpit.

### *Accumulation of Toxic Substances*

For many years, physiologists have attempted to associate fatigue with certain substances in the blood. At one time, many believed that lactic acid was the long-sought toxin.<sup>7</sup> Dill and his colleagues<sup>8</sup> have shown that the accumulation of lactic acid is related to fatigue but that, as an explanation of this phenomenon, such accumulation is more restricted than observers at first believed. Their experiments have revealed that the concentration of lactic acid in the blood remains a useful index to the degree of fatigue in one sort of activity, for example, that in which either the oxygen supply is deficient or the oxidative mechanism of the muscles is not competent to meet the demands placed on it. In studying a group of persons varying in athletic fitness or training, they<sup>9</sup> observed that in a famous Marathon runner there was no accumulation of lactic acid. In several untrained subjects, however, the accumulation of

lactic acid was very great. Those who were well trained were able to carry out the tasks with ease, whereas those in poor training who created large amounts of lactic acid were severely handicapped. The magnitude of the increase in lactic acid was closely related to the degree of fatigue, as indicated by other objective measures, such as the heart rate, respiratory rate and blood pressure, and by subjective evidence. That lactic acid is not the only factor was evidenced by the fact that many track records are broken by athletes in successive heats with large amounts of lactate in their blood. Furthermore, industrial workers doing heavy work, as well as miners at high altitudes, have been observed to have normal values for lactate in the blood. Other substances have been proposed as toxic factors in fatigue, such as ammonia and histamine, but further evidence is required to establish these theories.

#### *Exhaustion of Energy Reserves*

A great deal has been written about the exhaustion of such energy reserves as sugar as a causative factor in fatigue. Experiments indicate that in very exhausting work—in a Marathon race or industry—the administration of glucose is of considerable value in maintaining efficiency. In work with a bicycle ergometer, Christensen et al.<sup>10</sup> observed that a very low blood sugar was associated with exhaustion and even sensory impairment. These effects were rapidly counterbalanced by the ingestion of glucose, and the subjects could continue the work for an hour or more. In heavy work, the preferred fuel is carbohydrate. If heavy labor is continued for a long time without food, the diminishing reserve of carbohydrate is associated with a falling respiratory quotient, a reduction in efficiency, a decreasing concentration of blood sugar and the appearance of acetone in the urine. Subjects in poor physical condition have low reserves of energy and a reduced capacity for transforming energy. Unfitted or untrained factory workers, therefore, may benefit from glucose or other readily available fuel taken between meals. They seldom work hard enough to exhaust their stores of sugar and other reserves. The effects are chiefly on the central nervous system. It is difficult to explain the reports of benefits from the ingestion of glucose in more sedentary occupations.<sup>11</sup> During very long and exhausting flights at high altitudes, pilots are benefited by taking such foods as glucose, which is easily assimilated between meals. From evidence obtained on heavy muscular work, however, it is difficult to understand how a pilot could consume his entire carbohydrate reserve, since the amount of gross musculature involved is so small. It appears, there-

fore, that the exhaustion of energy reserves in a pilot could hardly be an important causative factor in fatigue.

In the field of mental work, it is even more difficult to explain how the ingestion of sugar might counteract the effects of fatigue, although it is well known that the nervous system is primarily dependent on carbohydrate for fuel. The metabolic cost of mental work is very slight indeed. Laird's<sup>12</sup> report that fatigue in students doing simple psychomotor tests is modified favorably by the ingestion of certain sugars, such as maltose, has not been confirmed by other workers. In carefully controlled experiments on the metabolic cost of mental work, Benedict<sup>13</sup> found that sustained mental effort for several hours required only the number of calories in half a peanut. Other experiments have shown that in mental work it is not the involvement of the nervous system that increases oxygen consumption, but the musculature and other parts of the body associated with attention and sustained concentration. Hence, the fatigue from mental work is due in part to the increased muscular tonus associated with sustained attention.

In spite of negative findings in studies of mental fatigue everyone is aware that subjectively it is a real phenomenon. Barcroft<sup>14</sup> suggests that mental fatigue, like chronic oxygen want, undermines normal self control, with consequent exaggeration of feelings and mental abnormalities. He recalls that, after prolonged strenuous work during the war, he broke down and cried for no apparent reason, as he did at the termination of his six-day stay in the low-oxygen chamber. It is common for anyone, after prolonged mental effort or continuous overwork, to be aphasic, quick tempered and lacking in self control to a marked extent, quite trifling experiences make one furious. Barcroft intimates that the mentally overworked person who eventually seeks medical or psychiatric advice is possibly suffering from chronic oxygen want. Overexertion breaks down the tissues, owing to insufficient oxygenation, and a prolonged rest is required before adequate restoration can take place. Barcroft concludes that one cannot at present answer one way or the other the question whether mental fatigue is due to oxygen want. The impairment may be caused by a defect in any link in the oxidation process. But one can state with certainty, he avers, that "a given strain produces a greater degree of mental fatigue as it would of muscle fatigue, when the oxygen supply is deficient than when it is ample." This observation is of significance for the pilot whose environment is known to be deficient in oxygen.

fatigue substances. Emphasis is placed on the variations in energy resources, such as oxygen and sugar, and, more especially, on several major contributing factors to fatigue, such as worry, personal maladjustments, lack of exercise, the effects of high altitude, poor selection of food, the excessive use of alcohol and tobacco, and certain factors in the cockpit of an airplane, such as noise and vibration. Finally, a study of fatigue in transoceanic airmen is discussed.

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factors, lack of exercise, the effects of lack of oxygen at high altitude, the wrong kind of diet and the excessive use of alcohol and tobacco are major contributing factors.

### *Exercise and Pilot Fatigue*

The trend of civilization from the earliest times has shown a close relation of the fitness of man and animals to their environment. If the environment changes, the animals must change to meet the new conditions. Airmen, to meet the requirements of prolonged sojourns at high altitude, must therefore attempt to adapt themselves so as to live comfortably and remain efficient under these conditions. In man's fight with the environment, the neuromuscular mechanisms have played a vital role. Under modern urban conditions, the muscles, lung surface and heart tissue are far in excess of what is needed for sedentary life. Unless the extra tissue is called into play, it atrophies and becomes a source of weakness. The highly trained athlete who suddenly stops training after leaving college is especially vulnerable to organ dysfunction. Large parts of the central nervous system are set aside for muscular activity, and this reserve must be used if it is not to become a source of danger.

The increase in emotional and mental disorders may also be related to the very great changes in modern, as compared to primitive, life. The glandular changes known to occur under emotional excitement, such as fear and anger, equip the organism for a struggle.<sup>21</sup> The secretion of adrenaline from the adrenal glands causes the blood pressure and heart rate to increase; the blood is directed from visceral activity to the muscles and brain; there is an increase in the rate and depth of breathing and a dilatation of the bronchioles of the lungs to facilitate the transport of oxygen to the arterial blood; the glycogen stored in the liver is released to provide extra fuel for the muscles; the pupils are dilated; and there is an increased rate in the coagulation of the blood in case of injury. All these changes have great significance in the survival of the organism in the event of a struggle. Under civilized conditions, however, there is less and less opportunity for an overt struggle, and there is less need for these physiologic changes. Continual emotional stress without overt activity may therefore have a cumulative ill effect on the efficiency of the organism in meeting situations involving stress. In piloting an airplane, there may be continual emotional stress, especially in adverse weather and over difficult terrain, without an excessive amount of physical exertion. At the end of the flight, the pilot should

attempt to obtain some form of physical exercise, to keep in condition.

There is some evidence of concrete advantages from routine exercise for airmen. The pilots in the Royal Dutch Airlines apparently derived benefit from routine gymnastics during a week following long flights from the Continent to the Dutch East Indies and return. In a study of 50 Pan American Airways pilots in Miami, Dr. John T. Macdonald<sup>22</sup> observed an increase of four points in the Schneider index by moderate yet routine exercise over a period of several months. The benefits derived from such procedures were especially apparent in the older pilots. Further controlled studies are indicated to demonstrate the value of regular exercise for airmen.

It is a common experience to find that a man in poor physical condition is easily exhausted by mental and physical exertion: he is irritable and likely to have morbid thoughts, petty ailments and poor judgment; he may have a sallow complexion and dull eyes; and he frequently complains of constipation, headache, nervousness and insomnia. On the other hand, it is equally common to observe in a man of good physical condition evidences of mental and bodily vigor, such as alertness, cheerfulness, high morale, healthy complexion and capacity for arduous mental and physical work. It is believed that these two conditions are but the outward expression of physiologic differences within the body. There are no tests available to predict whether a pilot will make a serious error of judgment or lose emotional control in a crucial situation. For the most part, however, it is safe to say that errors of judgment or emotional confusion are the reflection of a poor or rundown physical condition. For this reason, a pilot must maintain a high degree of physical fitness.

### *Effects of Altitude in Accentuating Fatigue*

It is well known that the important reactions in the human organism encountered at high altitude are due to the diminished partial pressure of oxygen.<sup>23</sup> There is no storage of oxygen in the human economy, as there is for other chemical substances like sugar and calcium, although the release of red cells by the spleen and bone marrow may be considered a reserve of oxygen in a limited sense. The blood is really the only storehouse, and its capacity is very limited. Hence, the body lives a hand-to-mouth existence and is dependent on a constant supply from the atmosphere. At 10,000 feet, a given breath of air supplies only two thirds as much oxygen as at sea level, and at 18,000 feet only half as much.

The average unacclimatized passenger is apt

to complain of certain physical discomforts while flying above 10,000 to 12,000 feet. In an extensive investigation carried out in experimental chambers at sea level and during prolonged flights at high altitude, the following reactions have been recorded voluntarily by the subjects and passengers.<sup>24</sup> The list is arranged in order of frequency and severity: slight frontal headache, which may become worse with increasing altitude; dizziness or vertigo on moving suddenly or in stooping over too rapidly; difficulties or irregularity in breathing and shortness of breath on exertion; digestive disturbances, especially gas in the stomach and in the intestines, and indigestion or slight nausea; slight sensory impairment on moving too suddenly, especially noticeable in alterations in vision; a tendency toward sleepiness or lethargy; and a sense of exhaustion and fatigue on exertion.

The response of the average passenger or pilot to high altitude may be influenced by a large number of variables. Since these factors are so essential in determining the altitudes where oxygen should be used and in answering other practical problems in civil aviation, a number of the more important ones are listed below. All these variables are either directly or indirectly related to the problem of pilot fatigue.

*Height attained.* There are great individual differences among the specific altitudes where the effects are first noticeable or become marked. Some persons may be affected at 8000 feet, and others at 16,000 to 18,000 feet. In a group of over 150 unselected subjects varying in age and physical fitness, in low-oxygen chambers at sea level during exposures of two to four hours' duration, the initial effects were significant in the average person at from 10,000 to 12,000 feet.<sup>24</sup> The effects may become quite marked at 14,000 to 16,000 feet and dangerous at 18,000 to 20,000 feet. The upper limit of consciousness in unacclimatized man appears to be about 25,000 feet.

*Rate of ascent.* In a series of experiments on rate of ascent, it was observed that if the high altitude is attained gradually, — that is, in an hour, — the effects are considerably less serious than during an ascent to similar altitudes within fifteen minutes. In a number of subjects who showed very poor responses following rapid ascents to 16,000 feet, a satisfactory acclimatization was made during repeated experiments in which the ascent was extended over one hour and fifteen minutes. During a slow ascent, the mechanisms of adjustment to the reduction in oxygen pressure have an opportunity to function. On the trans-Pacific flights, where from one to three hours may elapse

before the ship is leveled off at the desired altitude, slow ascents are physiologically favorable to the passengers and flight personnel.<sup>25</sup>

*Length of exposure.* Moderate altitudes of 6000 to 10,000 feet may be tolerated over long periods (eight to fourteen hours) without apparent ill effects. This does not seem to be so at 12,000 to 14,000 feet. Although the mechanisms of acclimatization may be effective at moderate altitudes, the opposite appears to be true at higher altitudes. Deterioration may set in, and the physical symptoms during the flight may be quite unpleasant. Older pilots find it advantageous to use oxygen at and above 9000 feet for flights of more than two or three hours' duration.

*Amount of physical exertion.* The effects of high altitude tend to be accentuated during exercise. This is of particular significance in stewards, whose chief activity involves the preparation and serving of meals and making up the berths while in flight. On this account, the other members of the flight crew should not make excessive demands on the steward during flights at high altitudes. Care should be taken not to make too sudden movements or to stoop over too quickly because of cerebral anemia or lack of blood and oxygen in the brain and the increased susceptibility to fainting. Passengers should be urged to remain quietly seated following a meal at high altitude, so that the blood will not be diverted from the digestion of food to the muscles. Also, the airmen might find it advantageous to arrange their meals aloft so as to relax for a short time following a meal before going on duty again.

*Roughness of air and sudden movements of plane.* Air-sickness becomes greatly accentuated at high altitude. Because of the combined effects of oxygen lack and rough air in interfering with the digestion of food, special precautions should be taken in the kinds of food ingested while one is flying under adverse conditions at high altitude.

#### *Importance of Pilot's Diet*

Among the factors that may affect the efficiency of a pilot, no one is more significant than his food. This is especially true during flying, because of the effects of oxygen lack on digestion. Several controlled experiments have been carried out on the effects of reduced oxygen pressure on the digestive processes. In studies with dogs, Delrue<sup>26</sup> observed a marked diminution of gastric secretion, lasting from two to three days, in animals taken from a low to a high altitude. Van Liere, Crisler and Robinson<sup>27</sup> found that the emptying time of the stomach was prolonged in proportion, so that at 20,000 feet the dogs had food

lower his ceiling, just as it would impair his performance in a track or crew race at sea level, owing to the unknown effects on the lungs and circulation. It also impairs his digestive processes and the assimilation of food. The airman is warned against smoking before breakfast and against the excessive inhalation of cigarette smoke at all times.

#### *Effects of Noise and Vibration and Other Variables in the Cockpit*

Certain variables in the cockpit of an airplane are contributing factors to pilot fatigue. These effects are less extreme in modern civil aircraft than in military planes. It should be kept in mind, however, that the noise and vibration in the cockpit are much greater than those in the passenger compartments of most civil aircraft.<sup>41</sup> Unfortunately, there are few controlled studies dealing with the effects of noise and vibration in aircraft on pilot performance and fatigue. Many pilots believe that these are significant factors, especially in flights of extended duration. A number of fatiguing influences that should be carefully controlled are as follows: the pilots' seats should be free of vibration and located conveniently near the controls and instruments; the navigating tables should be cushioned, to prevent excessive vibration; the cockpit should be well illuminated at night; radium paints should be eliminated on the dials because of the possibility of noxious effects from the radium; metal surfaces, which give rise to glare, should be eliminated; attempts should be made to reduce the static in the earphones; and the ventilation and temperature should be well controlled, to avoid extremes. All these variables may contribute to pilot fatigue individually or collectively. The flight surgeon should study every factor that affects the health or efficiency of the pilot. Most of these adverse conditions can be corrected by aeronautical engineers.

#### *Experimental Studies in Trans-Pacific Flights*

A study of fatigue in transoceanic airmen was carried out on a routine flight of the Pan American clipper between Alameda, California, and Manila, Philippine Islands, and return, to analyze the fatiguing effects of prolonged flights at altitudes averaging 9460 feet on 17 airmen and 11 passengers. The total flying distance of 14,141 nautical miles involved one hundred and twenty-two and one-half hours in the air. A series of physiologic, biochemical and psychologic studies were made at the various island stations. The following conclusions may be drawn from the data obtained on these airmen and passengers:

The subjects, both airmen and passengers, maintained a high degree of neurocirculatory efficiency throughout the flight, as judged by the individual items and composite score of the Schneider index. When the test was given in the basal state,—that is, before ascent,—none of the airmen tested below +7, a score frequently related to a significant degree of fatigue or unfitness in aviators. Of one hundred and forty-two tests in the basal state, only 2 subjects tested below +10, the average being +13, which is close to the mean of +14.8 for college athletes. The average basal state (fifty-four tests) was +11.5, only three tests falling below +7 throughout the flight. The mean score for the group at high altitude was +10.8. In a total of ninety-six tests given at a mean altitude of 9500 feet, only four fell below +7.

There appeared to be a general tendency toward low blood pressure as the flight progressed that was similar to the blood pressure observed in acclimatized workmen at high altitudes in the Andes. Six of the 8 airmen (the mean age for the group was thirty-two years) had systolic blood pressures below 110. The initial response to altitude usually showed an increase in pulse rate and an increase in systolic blood pressure, followed by a well-controlled fall to normal values if the subject remained at rest.

As the flight progressed, the pulse rate tended to show a greater increase after exercise and to take longer to return to normal. As might be anticipated, this was also true at high altitudes.

There was a consistent decrease in the Schneider indexes in Manila. This was related to the increased pulse rate caused by the high humidity and temperature of that region. After the subjects rested two days in Manila and slept in air-conditioned quarters, there was an improvement in the Schneider indexes. After a rest period of one week in Honolulu, there was a slight decrease in the mean Schneider index for the 8 airmen.

There was a tendency toward polyuria in these airmen, as commonly observed in athletes previous to competition, particularly in those who shared the greatest responsibility in handling the ship. As the flight progressed and the airmen became acclimatized, the polyuria diminished.

The partial pressure of oxygen and carbon dioxide in the alveolar air and arterial blood of these airmen was similar to values considered normal for acclimatized men at similar altitudes,

of the sensations of fatigue. In athletics, such as in crew or track, the transport of oxygen from the blood to the muscles is impaired, and it is for this reason that even small amounts of alcohol are detrimental and cut down performance by the fraction of a second necessary to win a race.

Recent research on the effects of alcohol has revealed a number of interesting facts for pilots and air passengers. Possibly one of the most direct effects of alcohol on the organism is that of diminishing the utilization of oxygen in the tissues. There is a close similarity between the behavior of a person suffering from acute oxygen deprivation on a mountain, in an airplane or in a low oxygen chamber at sea level and that of a subject under the influence of alcohol. The effect on the nervous system under both conditions is essentially the same—that is, a deficiency of oxygen is delivered to the tissue. At high altitude, there is a deficiency of oxygen in the inspired air, and under alcoholism there is a hindrance in the transport of oxygen from the blood to the tissues.

The frequent references to the similarities in behavior between the effects of alcohol and of oxygen want (anoxia) and the fact that acute alcoholism could be counteracted by breathing excess carbon dioxide led McFarland and Barach<sup>31</sup> to analyze the concentration of alcohol and lactic acid in the blood following the ingestion of standard amounts of alcohol in an oxygen chamber filled with air and at other times with excess oxygen (50 per cent) and excess carbon dioxide (2 to 5 per cent). The experiments showed that on the average both the blood alcohol and lactic acid were diminished during the breathing of excess oxygen and carbon dioxide as compared to the breathing of air. On the other hand, the alcohol was oxidized more slowly and the subjective effects accentuated when air deficient in oxygen was breathed. The experiments were repeated at 17,500 feet and 12,200 feet in the Andes, with similar results.<sup>32</sup> The significance of these findings for airmen is obvious. The effects of alcohol are greatly accentuated at high altitudes, and efficiency following the ingestion of alcohol is therefore impaired proportionally. The passenger who boards an airplane after drinking heavily may fall asleep quickly and forget his fears and worries. If the air is rough, however, he usually awakes and is more subject to airsickness. The pilot at that time, on the contrary, must be alert and efficient, and nothing should be involved to impair his nervous functions during the flight.

#### *Effects of Tobacco*

There are very few carefully controlled studies of the effects of smoking, and even less informa-

tion dealing with the effects of tobacco at high altitude. Modern advertising has tended to distort the facts regarding the effects of tobacco. The evidence from reputable university laboratories does not uphold the contentions frequently made that one brand of cigarette causes less acidity than another, or that any "lift" is due to an increase in blood sugar. It is obviously absurd that smoking necessarily goes with being a good athlete, explorer or aviator, as many cigarette advertisements imply.

The stimulating effect of tobacco is due to the nicotine, which is an alkaloid. Nicotine is poisonous, and in small quantities has an effect similar to other alkaloids (morphine, strychnine and cocaine). The commonly alleged soothing effects of smoking tobacco are due primarily to the nicotine. A number of carefully controlled studies indicate that smoking gives rise to the following reactions in the organism, largely through stimulation of the autonomic nervous ganglia: an increase in pulse rate, especially noticeable when one smokes before breakfast; an initial rise in systolic blood pressure, followed by a fall immediately after the smoking period, which may account for the dizziness often noticed by the inexperienced smokers; constriction of the blood vessels, particularly in the periphery of the body; a slight impairment in keenness of vision—since the eye is the most sensitive of the special senses, these effects are manifested in visual functions more readily than in hearing; inhibition of digestive movements of the stomach—it is from this effect that the smoker may temporarily allay his hunger; effects on the surfaces of the lungs, which give rise to breathlessness on exertion. There is some evidence that the carbon monoxide from smoking affects pilots adversely; although the amounts are small they are believed by many to be damaging at high altitudes and relatively innocuous at sea level.

During World War I, a series of studies was carried out on aviators relative to the effects of smoking.<sup>33</sup> The results indicated that in 75 per cent a single cigar or the inhalation of one or two cigarettes had definite though temporary effects on vision and caused an increase in pulse rate and a rise in blood pressure. The visual effects were manifested in terms of reduced visual acuity and ocular muscle balance. Only a few nonsmokers were studied. In these cases, some giddiness occurred at eighteen to twenty minutes from the start, and was accompanied by slight nausea.

It is therefore obvious that excessive smoking has a detrimental effect on the pilot's acclimatization to high altitude. It tends progressively to



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## THE TREATMENT OF WAR WOUNDS OF THE BRAIN\*

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IT is quite obvious that a discussion of the treatment of war wounds is most pertinent at the present time. This paper is designed to cover not only actual gunshot wounds of the brain but also similar injuries due to fragments from shells and from bursting bombs, the latter being probably even more frequent in this war than the ordinary types of wounds from penetrating missiles.

### PROPHYLAXIS

Since this subject is so obviously a war topic, a few remarks concerning what may be done by way of prophylaxis to lessen the severity of head injuries appear to be in order. In the first place, it would be most desirable if all soldiers could go into action with closely cropped hair. This would not only minimize the amount of hair that would be driven into the brain in penetrating injuries but would also prevent a great deal of infection of the lacerated scalp wound from the long hair, which becomes matted with blood and frequently incorporates itself within and contaminates the laceration. Furthermore, the shaving and sterilization of the area around any such wounds would be infinitely easier.

Secondly, tetanus toxoid has been shown to be a most valuable prophylactic agent and should be given to all soldiers and civilians likely to be involved in enemy actions. The usual dosage consists in 1 cc subcutaneously as a first injection and a second injection of the same amount two or three months later, a third injection after another two or three months is advisable. If it is known that this series of immunizing injections has been complete, 10 cc of tetanus toxoid should be injected subcutaneously at the time of injury; in the absence of complete immunization, 1500 units of tetanus antitoxin should be given immediately in all cases with compound injuries.

\*Presented at the annual meeting of the Massachusetts Medical Society Boston May 22, 1941.  
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Thirdly, the sulfonamides should be given by mouth at the earliest possible opportunity after a compound injury of any kind has been received. An initial dose of 6 gm of sulfanilamide should be given by mouth if it is possible for the patient to swallow, if the patient cannot swallow, it should be given through a nasal tube. Subsequent doses at four hour intervals, so that patients receive approximately 6 gm daily, should likewise be administered.

### GENERAL PRINCIPLES

It must be remembered that all penetrating brain wounds due to shell fragments, bullets, bomb fragments and so forth are compound fractures. One of the greatest essentials is to get these patients to a hospital or post where complete treatment can be carried out for their wounds at the earliest possible moment. So far as immediate or delayed surgical shock will permit, it is highly desirable that operative treatment, when it is indicated, be undertaken within twelve hours of the time of the infliction of the wound, and earlier if possible, since the sooner these wounds can be debrided the less the chance of subsequent infection and thus of complications, which so often either are fatal or produce untoward late effects ‡.

It must also be remembered that many patients, especially those who have multiple wounds elsewhere on the body or extremities, may first of all need treatment for serious shock. This must be combated in all possible ways by warmth, hot drinks, infusions of serum or plasma or transfusions of blood, the guarded use of small doses of morphine, and quiet and complete rest so far as this is obtainable. Infusions and transfusions can be carried out while the patient is being operated on; they should not be delayed too long before operation is undertaken. In addition to the care de-

‡It is possible that with the present more perfect methods of wound debridement together with the use of sulfonamide operation with primary closure may be delayed from twelve to twenty-four hours if necessary.

ing, has penetrated the underlying brain to varying distances, sometimes going in as far as one of the cerebral ventricles (Fig. 1); simple penetrating wounds, which are usually due to a rather large, single metal fragment that has carried in with it fragments of bone and other debris and has lodged somewhere within the brain, not infrequently penetrating the ventricle and sometimes crossing to the opposite side of the brain from that on which it entered (Fig. 2); pene-

tions, such as cerebrospinal-fluid leak or intracranial aerocele, may develop.

*The gutter type of wound and wounds due to a large, single penetrating fragment.* The operative treatment of wounds of the first two types may be considered together, since they are essentially similar in most of their aspects and in general require the same type of treatment.

After careful excision of the contaminated portion of the scalp, radiating incisions should be

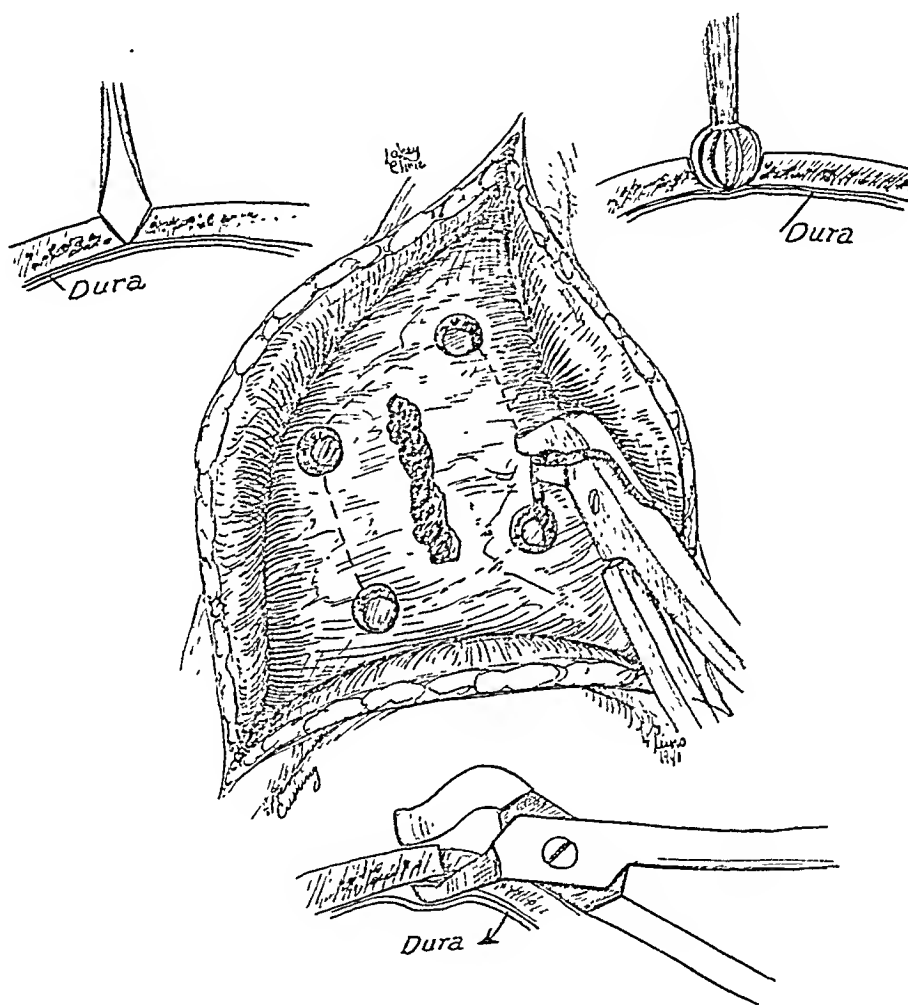


FIGURE 3. *Excision of the Bony-Penetration and Depressed-Skull Area by Bone-Cutting Forceps after Exposure of the Area by Reflection of the Scalp. (Modified from Cushing.<sup>2</sup>)*

trating wounds from multiple and often small fragments, particularly bomb splinters—this type of injury has been particularly prevalent in World War II; through-and-through or perforating injuries, which usually have a small wound of entrance and a much larger wound of exit, with a certain number of bone fragments carried in along the track; wounds involving one or another of the air sinuses, more particularly the frontal and ethmoid sinuses, in which subsequent complica-

made from the area of scalp laceration, usually in the form of a tripod, so that the flaps thus created may be retracted and an adequate exposure of the fractured area secured. The break in the skull is a relatively small round opening or a rather large, irregular hole in wounds due to a large metal fragment, and the bony defect is a long elliptical area in gutter wounds. Four burr openings are made surrounding this bony defect and including the depressed fracture area,

and these openings are connected with bone cutting forceps, a procedure that enables one to lift out the whole bony area intact and thus to expose the dura with either a small or a large perforation (Fig. 3). At this point, the procedure of choice varies according to whether or not an electrosurgical apparatus, together with adequate suction, is available.

If these two adjuncts are not at hand, a method similar to that employed during the first war, as advocated by Dr. Harvey Cushing, is in order. If the patient is under a local anesthetic, he is asked to strain or cough, and by this means considerable amounts of clots of semisolid contused brain may be expressed through the hole

being withdrawn from time to time and such material as has been sucked up into it is then discharged out of the field of operation (Fig. 4). In this way, all bone fragments and other debris may eventually be completely removed from the contaminated area in the brain. It is essential to remove every indriven bone fragment in this manner, and it is likewise advisable to remove the metal foreign body, which as a rule is found down at the bottom of the track, if this can be done without undue difficulty and without further damage to the brain. The metallic fragment can sometimes be located with the catheter, and a delicate, alligator forceps can then be inserted

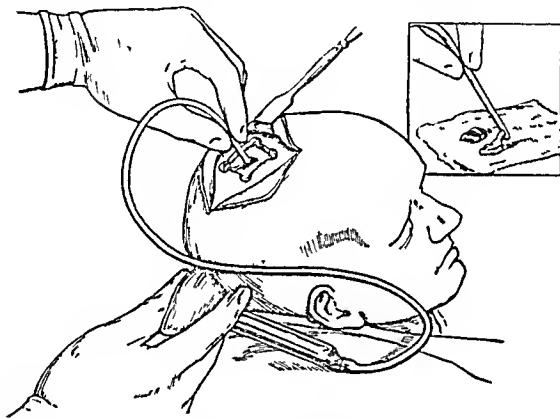


FIGURE 4 Catheter and Syringe Method of Debridement of the Track in the Brain (Cushing\*)

*The softened, disorganized tissue is sucked out, the bone fragments and other foreign bodies are palpated with the catheter and removed by delicate forceps*

in the dura, and such material may then be wiped gently away from the remainder of the wound. Indeed, small bone fragments may sometimes be thus extruded. A soft rubber catheter of suitable size is then inserted gently through the hole in the dura, and with this catheter as a means of palpation, bony fragments along the track of the missile are gently searched for and removed either by gentle suction with a syringe attached to the end of the catheter or by a grasping of the fragments with a delicate forceps and their extraction in this way. Gradually, as the catheter is inserted farther and farther in the track, the area is cleaned out by careful, not too vigorous suction on the catheter, thus, devitalized brain tissue, clots and other debris are drawn up into the catheter itself, the catheter

and the foreign body picked up and thus extracted. When the metallic fragment is of magnetizable material, it is often useful to insert a long, rounded nail down into the track in the brain so that it touches or nearly touches the metallic fragment. When this has been done, a powerful electromagnet is brought up to the end of the nail, and often the withdrawal of the magnet and the nail also withdraws the foreign body (Fig. 5). It is a long tedious process to clean out thoroughly a deep penetrating wound by the means thus described, and when this method is used, it is of the utmost importance not to disturb the dural edge and not to get out into normal brain outside the track created by the foreign body and bone fragments. At the end of such an operation, it is probably advisable to dust sulfanilamide or

sulfathiazole powder into the cleaned-out brain area; if the débridement is thought to be complete, if the operation has taken place within twelve hours of the injury, and if the patient can be followed for ten days or two weeks by the operator, primary closure should be made.

If an electrosurgical apparatus, together with strong suction, is at hand, a somewhat different procedure is preferable to the time-consuming and sometimes inadequate débridement possible by the catheter-suction method. Although it has

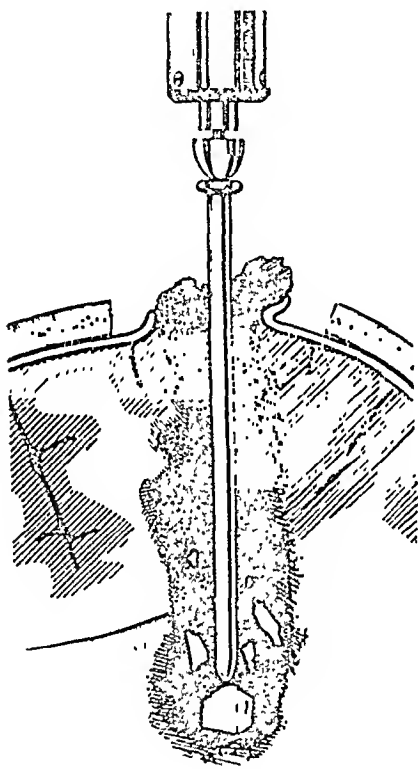


FIGURE 5. *Blunt-Nail and Electromagnet Method for Extraction of Magnetizable Metal Bodies.* (Horrax<sup>3</sup>; reproduced by permission of the publisher.)

not as yet been tried in combat or other war areas, I believe that the following procedure would be particularly applicable in wounds outside the motor and speech areas.\*

After exposure of the dura by the means already described, the membrane should be incised to a distance of perhaps a centimeter in a circular fashion outside the area of dural penetration, and then the whole track in the brain should be excised, together with its contained elements, in exactly the same way as a similar wound anywhere else would be excised. With the electrosurgical apparatus, an area slightly outside the actual track of the missile or bone fragments should be sealed off, that is, the blood

vessels on the surface should be sealed off around this area, and the brain incised in this coagulated area outside the track. Then, by a combination of strong suction, using a metal sucker, and with the electrosurgical coagulating current constantly applied to this sucker, one can clean out the soft brain surrounding the track, together with the clots and other debris (Fig. 6). If larger bone fragments are encountered, they can doubtless be taken out by the strong suction itself, or if they are too large for this, they can be extracted with delicate forceps. In this way, a core of tissue including a small amount of uncontaminated brain outside the track is completely removed by the combination of suction and electrocoagulation, the latter being employed to sterilize the area at the outside of the track as one proceeds. As the core of tissue is gradually removed, one can insert a flat spatula along either side of the cavity created, and thus débride the whole area under direct vision (Fig. 7). I am convinced that a much more complete and thorough débridement of all possible elements contained in the track can be accomplished in this way than by the older method. Any possible bleeding set up as this procedure progresses can be rapidly stopped by the electrocoagulation; finally, if a large foreign body requires removal from the bottom of the track, it can be seen and picked out very readily. When ventricular penetration occurs, the ventricle can be inspected and any debris removed from it. Again, as in the older method of treatment, wounds that have been completely débrided by the method just described should be closed primarily when patients are operated on within twelve hours after injury, after the local application of sulfanilamide or sulfathiazole powder within the wound.

When patients are operated on after the twelve-hour period following an injury, sometimes after one, two or even three days, the wounds show varying degrees of infection, which has sometimes gone on to an extremely foul-smelling herniation or fungous formation of the brain, with bone fragments and other debris extruding through the brain track. These wounds must be opened widely, and additional bone must usually be taken off around the area of penetration so that the dura can be incised in radiating fashion, thus relieving the almost certain constriction that exists at this point and is bottling up the infection inside. All devitalized tissue, bone fragments and other debris should be completely sucked away down into the track, which should be treated by open drainage of one form or another just like a brain abscess. It is my opinion that probably the best form of drainage in a case of this kind

\*I am informed by a neurosurgeon recently returned from England that this proposed method has been used there with excellent results.

is to insert gutta-percha tissue down to the bottom of the track, which is then packed widely open over this tissue with gauze. In any event, the track should be held widely open by some means, and in these cases it is probably best not to dress the wound for two or three days but to leave the original dressing, with its inserted

down to the diploe, from which granulations spring up and cover the bare bone much more quickly than if the granulating process were allowed to proceed merely from the edges.

*Multiple wounds made by small fragments.* It has been shown by British neurosurgeons during the present conflict that a very common type of

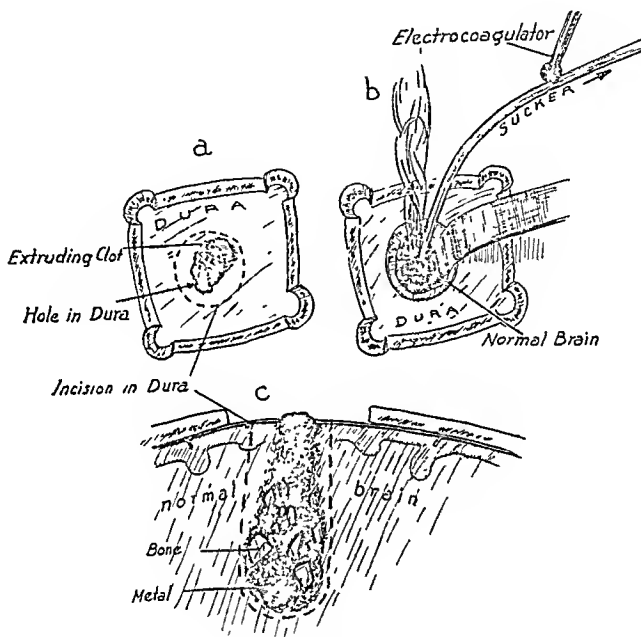


FIGURE 6. Procedure for Complete Excision of the Contaminated Track of Brain by Electrosurgery and the Suction Apparatus. (HORRAX; reproduced by permission of the publisher.)

*Incision of the dura (a) is made outside the track (dotted line), with subsequent removal of the whole area within the dotted line (c), after incision of the cortex just outside the penetrated area (b).*

drainage, in place so that a drainage track becomes firmly established. After that, the dressings can be changed either daily or every other day for the sake of cleanliness around the outside of the wound; as healing gradually takes place and infection subsides, the drain gradually extrudes and can be cut off a little each day. Finally, the area granulates, and if the exposure is wide, healing can be hastened by secondary suture or by some form of pinch grafts. If a wide area of bone has been exposed, it is sometimes an excellent plan to make perforations over this exposed area

head injury under existing conditions is the spraying of multiple small splinters of bomb casing into various parts of the body, including the head. These splinters are usually quite small, and because of their high velocity are almost red hot when they enter the body. Thus, they are sterile, and such material as may be carried in with them is probably rendered sterile. It has been found that much the best policy with these small fragments is to let them alone rather than to try to extract them operatively. Naturally, the scalp wound should be inspected and may need some

simple form of attention, either simple débridement and closure or perhaps only a simple dressing.

*Through-and-through wounds.* These wounds are usually made by machine-gun or rifle bullets that have passed from one side of the skull to the other through the brain; they are nearly always immediately fatal, but occasionally the patient survives and enters the hospital in fair condition. Very little need be done to these wounds as a rule. The wound of entrance is small and

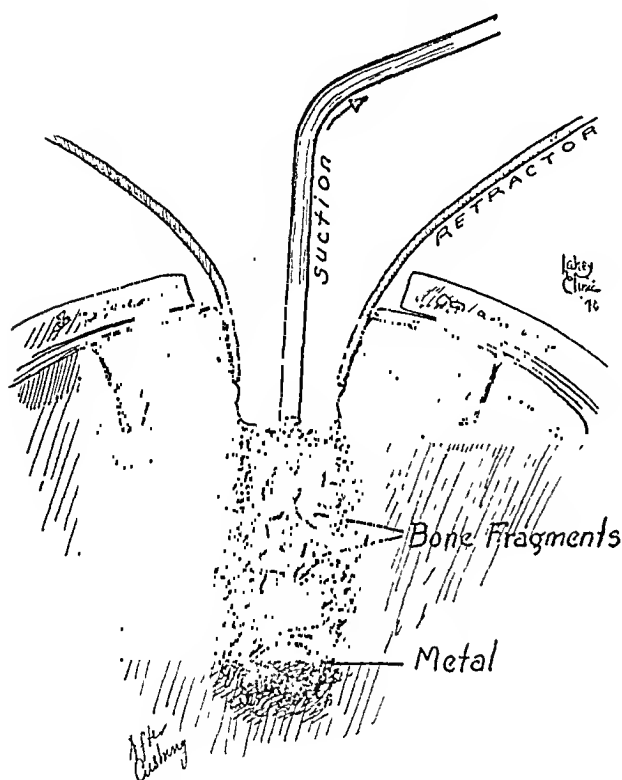


FIGURE 7. Detail of the Procedure Depicted in Figure 6. (Horrax<sup>1</sup>; reproduced by permission of the publisher.)

The brain edges are retracted, and the track cleaned out by suction under direct vision.

should be débrided in the usual way to a limited extent, unless x-ray study displays indriven bone fragments that are fairly easily accessible. The wound of exit, which is much larger than the wound of entrance, should be débrided locally, and any loose bone fragments present should be picked out. As in other contaminated wounds, the local use of sulfanilamide or sulfathiazole powder is indicated. If the injury is seen in the early stages, and if the patient is to be kept under observation by the operator, the wound may be closed after débridement, to effect primary union.

*Wounds involving the air sinuses.* These are extremely serious wounds because, in addition to the compound fracture involving the brain, there

is the open sinus, which cannot be closed and which affords a site of continuing infection for a long period. In wounds that have traversed the frontal sinus, the usual débridement of the brain should be performed, as in other types of penetrating wounds. Any general fragmentation of the sinus should be cleaned away as well as possible, such portion of the mucous membrane as has been obviously contaminated or is dirty being removed. If the wound is operated on within the first twelve hours from the time of injury, the dura should be closed, if possible, and the area should then be packed widely open, with gutta-percha tissue or rubber dam against the dura, and with gauze over this for packing. Another method is to close the scalp wound, leaving a drain down through the frontal sinus and coming out of the nose. If such a wound heals by primary union, much time is saved for the patient, but this procedure is far less safe than the open method.

The particular danger present with wounds involving the brain and air sinuses is a cerebrospinal-fluid leak. To prevent this complication, it is imperative, when possible, to close the dura after careful débridement of the brain. If such closure is not possible, a muscle implant may be used over the ethmoid cells when this area has been opened, or a vaseline gauze pack may be placed against the dura and uncovered brain when the wound has involved the frontal sinus. If the wound has been closed either by primary union or by packing off, and if a cerebrospinal-fluid leak develops, the patient must be reoperated on, and the fistulous tract from which the leak is coming sought. This is most frequently just above the cribriform plate of the ethmoid, and this area should then be sealed off with a muscle graft.

Another occasional complication of wounds through the frontal or ethmoid sinuses is the development of an intracranial aerocele. This is caused by the introduction of air through some portion of the dural laceration, and the patient as a rule begins to notice some increasing headache after a sneezing or coughing spell. X-ray study reveals the collection of air in one or the other frontal lobe. This air usually means a fistulous tract between a frontal sinus or the ethmoid cells and the brain. It must be sought and covered with a muscle graft to keep the aerocele from connecting with the ventricle and thus to prevent the development of a cerebrospinal-fluid leak. In all these cases, the continued use of sulfanilamide by mouth is advisable, to offset any possible infection.

## POSTOPERATIVE COMPLICATIONS

Patients who have had serious gunshot or shell wounds of the brain and have been operated on should have their wounds looked at carefully every day for a period of ten days to two weeks or longer if possible. If obvious infection is developing as shown by puffiness and reddening over the operated area, the wound should, of course, be reopened promptly and left widely open, gutta percha or some other rubberized type of tissue against the raw brain area being used. It may be wise in some cases to suck out further devitalized material from the superficial portions, at least of the track within the brain, and to treat the track just as one would a brain abscess, that is, by open drainage and by some smooth form of tissue next to the raw brain surface. It is a serious matter when these wounds do not heal by primary union and have to be opened up secondarily in this way but it is not by any means a hopeless matter, since many of them heal in time with careful treatment, frequently, even a herniation or fungus eventually granulates and recedes and the wound covers over with epithelium in the usual way. When a fungus develops from this source, or when the patient has been operated on late and it is necessary to leave the wound widely open from the start, the fungus should be covered with some smooth material, such as gutta percha, as stated before, and then surrounded by a doughnut of cotton over which the usual gauze dressing is placed. The doughnut is used to prevent pressure on the fungus which can only do harm, since it is not possible to keep the fungus from protruding and indeed it is not advisable to try to do so since such protrusion represents an effort of the brain to get rid of pressure. To prevent too great herniation of brain in this way, it may be advisable to do daily lumbar punctures to reduce the pressure to a certain degree.

Other acute postoperative complications include meningitis and diffuse encephalitis. These can be treated only by keeping the pressure down, so far as possible by frequent lumbar punctures and by the general use of the sulfonamides according to the type of organism involved.

Another immediate postoperative sequela, especially in patients who continue to be either drowsy or stuporous for a long time, is the collection of mucus in the air passages. This must be repeatedly cleaned out by suction because if there is not a free airway and if mucus gets down into the bronchial tree, there is every likelihood of an atelectasis or another pulmonary complication. It is imperative to have some form of suction apparatus immediately available on all wards where unconscious or semiconscious patients are situated, because the collection of mucus is a serious matter that must be attended to promptly and frequently.

With the late complications of head injury, such as brain abscess, post traumatic convulsions, headaches, dizziness and neuroses, this discussion does not presume to deal.

## SUMMARY

In the treatment of gunshot wounds of the brain, stress should be laid on such prophylactic measures as can be instituted, particularly the use of tetanus toxoid and of the sulfonamide drugs. The second important feature is the urgent necessity of getting patients quickly to a hospital where complete operative treatment can be carried out for wounds that require such treatment. In general, the earlier these wounds can be treated, the better will be the chance of preventing subsequent infection. Certainly, whenever possible, patients should have their complete operation within twelve hours from the time of injury. No avoidable delay for other purposes can offset the advantages of early operation. Finally, a careful, complete and painstaking débridement of the wound, both of the skull and of the brain, should be carried out, preferably by those who are well trained in this type of surgery.

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## WAR NEUROSES\*

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WAR neurosis is a three-dimensional problem. Its length can be measured only by time, which reaches from war to war. The casualties of World War I remain a tremendous medical problem, and the effect of the present European conflict is already bringing out evidences of nervous instability in the civilian population. Modern warfare includes men, women and children of all ages. Its breadth encompasses all the neurotic and psychopathic disabilities of civil life and includes practically every symptom in the whole category of medicine. Its height can be appreciated if one studies the report of the Administrator of Veterans' Affairs for 1940,<sup>1</sup> which reveals that 58 per cent of all patients being cared for in veterans' hospitals have neuropsychiatric disabilities. The economic aspect of the problem is appalling when one considers the money spent on training, compensation, pensions, hospitalization and treatment.

The war neuroses begin early. They are long drawn out and difficult to treat, and tend to increase for at least twenty-five years after the cessation of hostilities.

There are three definite points of attack on the war neuroses. First, in the selection of the men who are to enter military service, secondly, in helping to maintain the morale and caring for the mental casualties during combat service and, thirdly, in aiding the soldier during the period of demobilization toward rehabilitation and readjustment to civil life. The problem might well be considered in the light of these three outstanding phases of the soldiers' military experiences: mobilization, combat service and demobilization.

## MOBILIZATION

The local draft boards operated in much the same manner in 1917-18 as selective-service boards do today, weeding out the obvious misfits as they came along and depending more and more on the induction boards to make the final decision of fitness for service as time went on. The monotony of the routine examinations became apparent, and medical standards, which were set very high during the early part of the draft, were sustained with difficulty. The induc-

tion boards were called on to scrutinize the prospective soldiers more carefully, to eliminate the undesirable ones.

Approximately 3,500,000 men were examined by the neuropsychiatrists at the mobilization centers, and 69,394 were rejected because of some mental aberration. Approximately one third were mentally defective, one sixth were psychoneurotic, one tenth were psychotic, and about the same number were epileptic. The remaining one fourth were inebriates, drug addicts and victims of other neuropsychiatric instabilities. As the war continued and more men became engaged in combat service, the mental casualties increased to a rather alarming extent, and finally a request came from abroad that a more careful selection of men be made on this side before sending them overseas for active service.‡

The physical stresses and mental strains of camp life served as a test for the mental stamina of the soldier, and a screening-out process eliminated many from service overseas. The intimate social contacts of camp life, the arduous military training and the exacting disciplinary measures constituted an experience that was too taxing for certain prospective soldiers to meet adequately. The adaptations that had been built up to civil life began to break down. The men whose intellectual endowments were definitely limited were looked on by their comrades as being stupid, and by their officers as being indifferent. The soldiers were right. But it was the duty of the officers to train these men; hence they were rebuked, humiliated, assigned to kitchen police and other unpleasant tasks and punished; finally, in revolt, they became defiant, went "AWOL," and landed in the guardhouse. Usually, the offenders were seen and examined by the psychiatrist and eventually rejected as being unfit for military service.

It is of interest to note in passing that the psychologic examinations given to groups of perhaps a hundred or more men at one time indicated that intellectually it was the men who fell in the low 10 per cent that made up a large number of the chronic offenders, and it was the high 10 per cent from which many of the noncommissioned officers were recruited. These tests were found to

\*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 22, 1941.

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‡The following extract is from a cablegram sent by General Pershing on July 15, 1918: "Prevalence of mental disorders in replacement troops recently received suggests urgent importance of intensive efforts in eliminating mentally unfit from organizations of new draft prior to departure from the United States."



give a very adequate measure of the relative intellectual equipment as well as the practical ability of the soldiers, and there was a fairly close correlation between their test scores and their achievements.

There were the shy, sensitive, timorous lads who found the bayonet drills and the practice of running the dummies through under the direction of the enthusiastic masters of military technique a bit too realistic, and who became the victims of their own vivid imaginations and undue sensitivity. Some developed physical symptoms such as nausea, vomiting, fainting, tremors and insomnia, others developed the more serious mental symptoms that are so common in the anxiety states. Some men became morbid and depressed with definite psychotic symptoms. Every type of mental disorder was precipitated by the inability of the predisposed to meet the demands of camp life. These experiences did not cause the disease, they simply brought in existing instability to the surface where it could be recognized.

Such were the cases that were returned from the camps to civil life or held for noncombatant service. A recognition of these potential neurotics prevented them from developing a more serious mental disability overseas, where the problem of care and treatment would have been tremendously increased.

It is difficult to reconcile the rather superficial neuropsychiatric examinations that are being made at the present time, — limited to about seven minutes for each man, — with the gravity of these casualties both from a military and from an economic point of view. It was recently stated that adequate psychiatric examinations which would weed out the potential neuropsychiatric disabilities would save the Government \$500,000,000 for every million draftees.<sup>3</sup> It has been estimated that every psychotic soldier who breaks down in the Army costs the Government \$30,000 from the time of the onset of his disease until his death.<sup>4</sup> If psychiatrists can be hired at the rate of \$15 a day it takes but a little mathematical reckoning to determine that if one psychiatrist picked out one potential psychotic every six years, he would save the Government his salary.

#### COMBAT SERVICE

The neuropsychiatric disabilities resulting from active military service represent the war neuroses of the American forces of the first war and the shell shock of the British. They are made up of so many and so varied heterogeneous groups that it would be a time-consuming task of but little value to define the limitations of each. In the order of their frequency, and including a very

large percentage of all the neuropsychiatric disabilities, they are neurasthenia, conversion hysteria, anxiety states and the psychoses.

The underlying mechanism of the disability is pertinent to this discussion. The war neuroses represent a group of neuropsychiatric disabilities incurred in military service and resulting, on the one hand, from conflict between acquired social attitudes — such as loyalty, patriotism, honor and the maintenance of one's personal customs and traditions, as well as those of the army, regiment and company, all of which Trotter includes under the term 'herd instinct' — and, on the other, from the instinct of self preservation. These sets of dynamic forces, although always present are under ordinary conditions not in serious conflict, inasmuch as the 'herd instinct, or the so called 'social drive,' is allowed to operate more or less freely, unhindered by any interference from the instinct of self preservation. Only under conditions such as war, floods, earthquakes and panics, in which there is a direct threat to one's existence, does the instinct of self preservation assert itself and become a dominating force.

The purpose served by the neurosis, as stated, is that of protection, and to be adequate and fulfill the purpose for which it is psychologically designed, the neurosis must protect both the soldier's ego and his physical being — that is, it must permit him to escape from the intolerable situation created by the impending dangers of war on the one hand and to accomplish this without loss of self respect on the other.

Since neurosis has been recognized as a medical problem, with symptoms comparable to those of any other illness and since neurosis has been accepted as a medical entity by those in authority, both medical and military, and by the soldier, the public and the press, it has not been difficult for the soldier to accept his disability as a way out of a difficult situation. Consequently, a neurosis solves the conflict between the herd instinct, which drives the soldier on to perform his military duty and to live up to those socially acquired traditions and his personal ideals of what he would like to be and the instinct of self preservation which is constantly threatened by the dangers of pursuing the paths of duty.

It is of interest that neurosis was rarely observed in men at the front or in those who had been wounded and were in base hospitals. However, a certain number of wounded men developed states of anxiety as the time approached for their discharge from the hospital especially if they were assigned to active military duty.

Neurasthenia, the anxiety states and the psychoses had a fairly equal distribution among all

those engaged in military service—officers and soldiers alike. The so-called “conversion hysterias,” however, were found in an overwhelming degree in the more suggestible, less well intellectually endowed soldiers, and were infrequently seen in the officers. These physical manifestations of mental conflict, such as the paralyzed arm or leg, functional blindness, deafness, aphonia, and the more violent tremors and muscular twitchings, represented what might be termed a rather crude method of solving the conflict. In other words, the average soldier confronted with danger met the situation promptly, decisively, and without any great struggle to carry on, whereas the neurasthenic did not. He developed a syndrome with such symptoms as fatigue, insomnia, battle dreams, anxiety and depression, frequently lasting over a period of weeks or months before completely incapacitating him. Many of these men went in and out of the front-line trenches month in and month out until they finally reached the breaking point.

Treatment of the conversion hysterias was usually not difficult. The patients responded readily to methods of suggestion, such as the faradic battery, isolation and hypnosis. However, it was found from experience that as a group they had little to contribute to military service. The other types of cases—the neurasthenias, anxiety states and the compulsive and obsessional neuroses—invariably required long periods of rest and prolonged psychotherapy. It was the experience of the medical officers in the American Expeditionary Force that severe cases of war neuroses that required evacuation to base hospitals were rarely good risks for further front-line service. The origin and purpose of the neurosis is to protect the patient from a situation which he is inadequately prepared to meet because of a poorly organized nervous system and a poorly integrated personality make-up. To return these men to the same situation that created the initial breakdown was a hazardous undertaking. The experiences of the American Expeditionary Force and those of the British Expeditionary Force during the first war were not particularly different from the experiences of the British at the present time.

Debenham, Sargent, Hill and Slater,<sup>6</sup> in a recent article dealing with 1550 cases of neuroses or psychoses in members of the armed forces, state:

In the early months of the war, cases were largely those men who should never have been regarded as fit for military service. . . . At evacuation of Dunkirk another type predominated, acute anxiety or exhaustion syndromes in men of apparently normal personality,

who had not broken down until placed under considerable strain. . . . It is useless to send a man back into army life merely because he is symptom free if he is liable to break down under small strain. An assessment must be made of the personality and of the strains that it is able to support. The longer the neurotic reaction is allowed to persist, the more difficult it is to deal with.

In contrast with American and British attitudes toward the war neuroses, I quote from a book by Martin Gumpert,<sup>7</sup> which presents the German medical and military point of view:

War hysteria and “trembling” are mere cowardice, masquerading as sickness. It is wrong to cater to war-hysterical people. How then shall the army administration treat them in the future? First, and at once, *they must be brought to a war hospital. Their stay in the war hospital will be short and the hospital not too close to home. They must realize that they are to face conditions which will not at all accord with their wishes. Unfortunately, it is not possible, for obvious reasons, to send back to the front men who cannot be cured of their nervousness in the war hospital. Normal men would not understand the reasons why such “poor sick people” should be left in the trenches; morale would suffer. Obstinate cases must be united in special squads and sent to places where they can be put at physical work, without consideration for their nervousness. This work must not be too far from the front, but must be right up in the danger zone—road building, trench work, etc., where the risk is no less great than for the soldiers in the front lines. These men must be forced, without consideration for their neurosis, to those kinds of work which normal individuals might do, because such “trembling” cannot be counted as a sickness. Therefore, war-hysteria, even should it increase, will not be reason enough to remove anyone from the war zone; indeed the strongest pressure must be used upon him to make him fulfill the tasks assigned to him.*

It is obvious from American and British experience that the war neuroses as they develop in line of duty represent an extremely difficult type of medical casualty and that therapy should be applied at the earliest possible date not too far removed from the scene of conflict. A fairly large percentage of patients can thus be rehabilitated in a relatively short time and sent back to active service. The cases that do not respond to this type of therapy and require evacuation to base hospitals can usually be rendered symptom free, but it is probably not wise, from a medical point of view, to return the patients to combat service. Many of these men were able to carry on in the Section of Supplies, and rendered a valuable service. However, thousands during the last war (approximately 3000 psychotic and 5000 psychoneurotic soldiers) had to be evacuated to the United States.

## DEMILITARIZATION

It is my opinion that more men suffered from artificially created neurotic conditions during the period of demobilization than from neuroses that developed on the battlefields of France. Literally thousands of men passively succumbed to a life of dependency on the Government and eventually became incapacitated for a self respecting, independent existence, owing very largely to the oversolicitous service organizations and the unwise distribution of pensions brought about by national sentimentality and political pressure. During the period of demobilization, various national organizations, with the best of intentions, asked soldiers to make claims for disabilities that could by no stretch of the imagination be considered medically valid. It was not for incapacities already existent but in an anticipation of what might possibly occur that many of these claims were made. These men became the unwitting victims of demoralizing subsidies from a paternalistic government.

When men are paid for being sick and penalized for getting well, the medical profession has little or nothing to contribute. The danger of building up a large group of veterans showing pseudoneuroses or compensation neuroses was entirely ignored. There is perhaps no period in the whole experience of military service that is more critical for the future happiness and efficiency of the soldier than this period of demobilization. It is also important to the Government from an economic standpoint, as well as for the preservation of man power. Psychiatry could have contributed much during this period for the welfare of both men and the Government. There was no real need for hurry during demobilization. It might have been an opportunity for carrying out a well co-ordinated plan for reorienting a certain group of men to civilian life after their war experiences. As history shows, it was anything but that. It could not be done through compensation alone.

Another phase of demobilization that contributed to many maladjustments later on was the hurried, haphazard procedure of placing men in civilian training. Many men were encouraged to take up some form of training for which they were intellectually unfit. Being ambitious, many were lured into attempting to become doctors, lawyers, public accountants, artists and engineers, and into other professions for which their education before or during the war in no way prepared them. They gave up their prewar occupations and lost interest in the pursuits that they were equipped to follow. Failure resulted from the great gulf that existed between their ambitions and their abilities. It is hoped that such obvious mistakes will be eliminated during the next period of demobilization. It is one aspect of the whole situation from which the ex soldier should be safeguarded.

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In conclusion, I repeat that the war neuroses represent one of the most significant military and economic problems with which the Government has to deal. Every effort should be made to select men with care, to organize medical centers where adequate treatment can be administered during combat service, and to give careful consideration to the problem of rehabilitation after military activities have ceased.

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## BLOOD AND BLOOD SUBSTITUTES IN THE TREATMENT OF HEMORRHAGE, SECONDARY SHOCK AND BURNS\*

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PHILADELPHIA

SECONDARY shock may result from extensive operations, from the severe injuries of civil accidents or military wounds, or from burns, severe infections, profound anemias and other conditions.<sup>1</sup> Loss of blood, emotional stress, prolonged exposure to cold, and physical and nervous exhaustion may all be contributing factors. The cycle of deranged function that characterizes the shock state essentially involves injury to and loss of tone of the blood capillaries, loss of fluid and plasma proteins through the capillaries, and tissue anoxia (oxygen-deficiency). Unless this vicious circle can be broken, circulatory failure and death ensue. The mechanisms involved have been well summarized by Moon,<sup>2</sup> who has contributed extensively to their elucidation. The following is quoted from Moon<sup>3</sup>:

Endothelium is delicately sensitive to lack of oxygen, to metabolic products, cytoplasmic substance, bacterial toxins and to a wide variety of chemicals and drugs. When affected by any such substances, the endothelium becomes relaxed, atonic and abnormally permeable to blood plasma. The sequestration of blood in dilated capillaries reduces the effective blood volume, and the leakage of plasma into tissue spaces lowers the total blood volume. This creates a disparity between the volume of blood and the volume-capacity of the vascular stream bed. This disparity, if not compensated, causes circulatory deficiency.

Compensation is accomplished through responses activated probably by impulses from the carotid sinus. Activity of the sympathoadrenal system causes constriction of peripheral arteries, the discharge of reservoir blood from the spleen into the systemic circulation and stimulation of the heart by the adrenal medullary hormone. So long as the mechanism of compensation is effective there is no marked decline in the blood pressure, but the latter is maintained at the expense of volume flow which is reduced markedly. This stage of shock can be recognized by the presence of hemoconcentration. A progressive decline in the blood pressure signifies that compensation is failing and that the end is near. It is a sign of departed opportunity.

Capillary atony in extensive areas reduces both the total and the effective blood volume and leads to a reduction of the volume flow. This reduces the delivery of oxygen to the tissues. When the supply of oxygen falls below physiologic limits, it augments the capillary atony. Moderate lack of oxygen causes dilatation and hyperpermeability of capillary walls. This effect introduces a self-perpetuating quality which operates as a vicious circle and leads to irreversible changes.

Successful management of shock requires early recognition and effective measures for breaking the vicious circle. These will be directed toward removing the cause, toward increasing the blood volume and toward relieving anoxia. Saline solutions and artificial colloidal solutions are ineffective or objectionable. Transfusion of whole blood, except after serious hemorrhages, is not advisable. The ideal substance is that which has been lost from the circulation—plasma. Infusions of human plasma or serum should be given when hemoconcentration indicates impending circulatory failure and before the arterial blood pressure declines. Oxygen should be given by inhalation to counteract anoxia.

Although there are still points of controversy about the relative importance of the various mechanisms of injury that lead into this cycle of shock, there is general agreement that the critical factor whose correction is the most immediate necessity is the depletion of the volume of circulating fluid. The volume of the circulating fluid must be restored to normal as quickly, and maintained as nearly normal, as possible. For other measures in the treatment of shock, more general discussions should be consulted.<sup>4-7</sup>

For restoring the circulating-fluid volume, intravenous infusions of various fluids made isotonic by diffusible solutes, such as sodium chloride and glucose, have been tried. In general, such fluids offer only temporary relief because of the rapid loss of the added solute from the circulation into the extravascular fluids. Various fluids containing nondiffusible solutes, such as gum acacia, hemoglobin and bovine serum albumin, have been or are being tried. These fluids may have notable advantages from the standpoint of availability and low cost. In general, however, they result in the introduction of foreign substances into the circulation, and no one of them has yet passed successfully through the stage of clinical proof of efficacy and harmlessness. One of these artificial solutions may, of course, ultimately prove to have wide usefulness.

The ideal physiologic corrective for the depleted circulating-fluid volume of secondary shock in man is obviously human plasma or serum. Both plasma and serum have had wide trial in experimental shock (dog serum or plasma being employed in dogs),<sup>4, 8-10</sup> in postoperative clinical shock, and in that following civil accidents, burns or war wounds (human serum or plasma being used).<sup>6, 9, 11</sup> There is general agreement among workers in Great Britain, Canada and the United

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States that either plasma or serum, properly prepared and administered, is an optimal corrective for the depleted circulating-fluid volume of shock.\*

There has been a great deal of discussion about the relative merits of plasma and serum for the treatment of shock. It seems that for the purpose of restoring circulating volume there is little difference between them; intravenous infusion of either is efficacious. The advocates of plasma point out that it is possible, by immediate drying of the plasma from the frozen state, to preserve the prothrombin and complement as well as the globulins and albumin of the plasma, and that more plasma than serum can be prepared from a given volume of blood.<sup>11-13</sup> The advocates of serum point out that, since the essential value of the blood proteins in the treatment of shock lies in their colloidal osmotic pressure, the additional preservation of prothrombin and complement has little practical value under the circumstances in question, and that, moreover, serum is easier to prepare and requires somewhat less exacting conditions of administration.

A second point of controversy between the partisans of serum and those of plasma has been with regard to reactions on injection. The consensus seems to be that plasma, either fresh or regenerated after drying from the frozen state, may be given intravenously with no more fear of reaction than in the transfusion of whole blood. Serum that has been aged several weeks before administration or before drying for preservation may be administered with equally little risk of reaction. Some specimens of serum that have been preserved by drying shortly after taking off the clot have caused reactions, but these reactions seem to have been due to special conditions quite outside usual practice in preparing serum.

In current practice, serum and plasma for the treatment of shock are prepared in large pools representing many donors. Such pooled plasma or serum may be administered intravenously without regard to the blood type of the patient.

The question of whether serum or plasma should be concentrated, normal or diluted when administered in shock requires discussion. In general, this decision apparently depends on the condition of the patient; the aim should be to restore as nearly normal conditions as possible. If shock is complicated by concussion, as in accident or war cases, there may be a definite advantage in giving hypertonic, concentrated plasma or serum, which withdraws fluid by osmosis from the central nervous system and tends to restore the circula-

tion to normal.<sup>14, 15</sup> If the patient is markedly dehydrated, a condition that may occur after burns or military wounds, there may be advantage in giving dilute plasma or serum in large volumes. In other circumstances, isotonic plasma or serum may be indicated. Estimation of hemoconcentration or hemodilution by hematocrit readings, hemoglobin determinations or otherwise may afford useful indications of what is required. A rising hemoglobin percentage or an increase of the cells-to-plasma ratio indicates hemoconcentration due to loss of plasma through the capillary walls. When there has been extensive loss of blood, it may be well to follow the immediate treatment of shock by transfusions of whole blood.

It is of course simpler and more economical when practicable to keep plasma or serum in the liquid state. However, under conditions requiring prolonged storage or transportation, as for war purposes, and when concentration is desired, preservation by drying presents great advantages. Drying from the frozen state is generally conceded to be the method of choice, and is the method currently used in the preparation of dried plasma and serum for war purposes.<sup>5, 7</sup>

Several procedures and apparatus currently used for drying from the frozen state have been described under the terms "lyophile," "cryochem"<sup>16</sup> and "desivac."<sup>17</sup> In each of these processes, the plasma or serum is frozen and then desiccated in a vacuum at a rate sufficient to keep it frozen by the continued cooling incident to the loss of the latent heat of vaporization. The three procedures differ essentially in the means used to remove the water evaporated from the material undergoing desiccation. In the lyophile process, the water vapor is condensed as ice in a bath kept cold by dry-ice; in the cryochem process, the water vapor is absorbed by Drierite, a specially prepared, regenerable calcium sulfate desiccant; in the desivac procedure, the water vapor is trapped in the oil of the large vacuum pumps used, whence it is continuously separated by centrifugation. For drying small volumes, that is, up to about a liter daily, the cryochem apparatus has proved to be the most economical in operation, and for larger volumes, that is, from one to many liters daily, the desivac apparatus is the most efficient.

For use in the present war, large volumes of liquid and dried human serum have been and are being prepared in Great Britain. In the months before this undertaking was organized,<sup>18</sup> much liquid plasma was prepared in Greater New York, through the collaboration of the American Red Cross and the Blood Transfusion Betterment Association, and shipped to England. Large amounts

\*Concentrated solutions of human serum albumin, now under investigation by Drs. E. J. Cohn and Charles A. Janeway, may prove to have distinct advantages.

of liquid and dried serum are being prepared in Canada for war purposes. Large volumes of dried plasma are now being prepared in this country, with the collaboration of the American Red Cross, for the use of the United States Army and Navy.

For civil use on a small scale, plasma may be prepared directly from fresh whole blood, or plasma or serum may be prepared from blood stored in blood banks until the corpuscles must be discarded. Because of reactions Strumia et al.<sup>11, 12</sup> warn particularly against the administration of fresh (twenty-four to forty-eight hours' old) serum or serum vacuum-dried when fresh; such reactions have rarely been encountered with plasma or with serum held for several weeks in the liquid state before administration or drying. Human plasma and serum prepared by several of the large manufacturers of biologicals have recently been put on the market, but their price is high, owing to the cost of collecting and preparing such products.

#### SUMMARY AND CONCLUSIONS

The role of blood and blood substitutes in the treatment of hemorrhage, secondary shock and burns is briefly discussed.

Human plasma and serum are the most effective agents for restoring the volume of circulating fluid to normal in cases of shock and burns, as well as of hemorrhage in the absence of excessive bleeding.

Although serum and plasma are most easily and economically preserved in the liquid form,

drying from the frozen state by the lyophile, cryochem and desivac processes is recommended for war purposes and under conditions requiring prolonged storage or transportation.

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## MEDICAL PROGRESS

ISOIMMUNIZATION IN RELATION TO INTRAGROUP  
HEMOLYTIC TRANSFUSION REACTIONS\*

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POST-TRANSFUSION reactions of the hemolytic type are most commonly ascribable to intergroup incompatibilities. These accidents have occurred because of mistakes in grouping the blood of the donor or the recipient, and occasionally<sup>1,2</sup> have been due to the use of a Group O (so-called "universal") donor whose natural isohemagglutinins were unusually potent—that is, effective in high dilution. Probably the commonest error in grouping is failure to recognize persons of Groups A<sub>2</sub> and A<sub>2</sub>B because of the low agglutinability of cells containing the A<sub>2</sub> substance. Weak anti-A serums may fail to cause any agglutination of such cells even when unusually sensitive techniques are used; consequently, such persons would be mistakenly allocated in Group O or B, and under certain conditions accidents would be expected whether these persons donated or received blood that was actually incompatible.

But in addition to such intergroup causes of reactions, there have been reports of post-transfusion reactions when bloods of homologous groups have been transfused, and when the preliminary tests have been made by experienced observers using potent serums.<sup>3,4</sup> Reactions under such circumstances have usually occurred in patients who have had repeated transfusions, the first or first few having been uneventful; such reactions have also been observed with unusual frequency following primary transfusions given to pregnant or post-partum women.<sup>5-10</sup> Some recent disclosures coupled with long-known facts afford a plausible explanation of these intragroup incompatibilities. It is the purpose of this review to consider the probable mechanism, which is based on isoimmunization with certain antigenic components of human blood.

## ISOIMMUNIZATION

Isoimmunization was successfully accomplished by Ehrlich and Morgenroth<sup>11</sup> as early as 1900. Isohemolysins were readily produced in the goat

by injecting erythrocytes of other goats. These immune, not normal, isoantibodies hemolyzed the cells from the goats that furnished the original inoculum and the cells of some, but not all, other goats. The serum did not contain an autolysin—it did not affect or combine with the cells of the animal in which the antibody was formed. These observations were of basic significance in that they showed the possibility that a considerable number of different antigens might exist in similar cells of different individuals in a single species. They also indicated that an animal will not produce antibodies to antigens that are present in his own blood. This principle was expressed concisely by Ehrlich and Morgenroth<sup>11</sup> in the phrase *horrer autotoxicus*. It is true that an animal can form antibodies against some of his own proteins or other components of his tissues, for example, the substance of the crystalline lens, casein<sup>12</sup> and an alcoholic extract of brain,<sup>13</sup> but these materials are blood-foreign and thus satisfy one of the primary prerequisites for antigenicity. The preliminary report by Kidd and Friedewald<sup>14</sup> on a natural antibody found in adult rabbits is of interest. This thermolabile antibody, not present in young rabbits, fixed complement strongly in the presence of saline extracts of normal tissues from a rabbit, rat, mouse, guinea pig or chicken. Extracts of liver and kidney were especially rich in the reactive substance. Immune isoantibodies have been produced in other animals and fowls (Wiener<sup>15</sup>).

## GROUP-SUBSTANCES A, B AND O AS ISOANTIGENS

Isoimmunization in man cannot, of course, be studied with the delicate and thorough experimentation permissible in animals, and observations must perforce be limited to cases of inadvertent mistakes in transfusion and to events that may follow or accompany pregnancy when the parents present certain incompatibilities of their bloods. Thomsen<sup>16</sup> did attempt to immunize men by intramuscular injections of incompatible blood, but no significant rise in isoagglutinating titer was observed (one should note the findings of Biancalana and Tenet,<sup>10</sup> however). This apparent evidence against the isoantigenicity of the

\*All articles in this series will be published in book form, the content volume is *Medical Progress: Annual, 1940* (Springfield, Illinois: Charles C. Thomas Company, 1941. \$4.00).

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A and B group-substances is, however, outweighed by the positive evidences mentioned below. Thomsen's negative result is probably attributable to the relatively small quantity of blood injected. Possibly, the route of injection had some influence; as an analogy, the report that rabbits treated with suspensions of streptococci produce anti-C much more readily following intravenous than subcutaneous injections<sup>17</sup> may be mentioned.

It is highly probable that the case reported by Thalhimier<sup>18</sup> in 1921 is an example of the isoantigenicity of Group-Substance B. A boy received 300 cc. of his father's blood; cross-matching had revealed no incompatibility, and only a mild febrile reaction ensued. Eighteen days later, without further tests, the father again served as donor; an alarming reaction stopped the transfusion after 150 cc. of blood had been introduced. Subsequently, the bloods were grouped; the son was found to be an O and the father a B. Although no agglutinative titers were determined, one may surmise with confidence that the anti-B normally present in Group O plasma (with anti-A) was too weak to be detected by the ordinary test, and that the primary transfusion of Group B blood served as an immunizing stimulus leading to a probably marked rise in the titer of anti-B, which thus intensified the incompatibility.

Further evidence that A and B are isoantigenic appears in Jonsson's<sup>19</sup> finding that the maternal isohemagglutinins  $\alpha$  and  $\beta$  are of higher titer when the corresponding antigen, A or B (not present in the mother's blood), is present in the blood of the fetus than when it is absent (transplacental isoimmunization).

Rø<sup>20</sup> observed the development of immune anti-A agglutinins in a Group O patient given Group A blood. Wiener<sup>21</sup> has recorded 2 cases in which powerful immune anti-B (sixteen times the average titer) was produced; the recipients were O and A, the donors B and AB. Another recent case of isoimmunization of a Group B patient given AB blood is also described in detail. The anti-A titer rose from 1:4 immediately after the transfusion to 1:512 on the eighth day. There was no significant difference in titer whether the tests were done at 37°C. or in the icebox, whereas natural isoantibody as a rule reacts more strongly at low temperature. Prior to this report, the only case of isoimmunity involving these subgroups was the weak "irregular" ( $\alpha_2$ ) agglutinin found by Landsteiner, Levine and Janes<sup>22</sup> to have developed, or more probably to have increased in titer, following intragroup transfusions. It was slightly less active at 37°C. than at room temperature. A second transfusion from the same donor

was not followed by symptoms, although the agglutinin was present after the first transfusion.

Davidsohn<sup>23</sup> has argued logically, principally from circumstantial evidence, that the subdivisions of Groups A and AB—the Subgroups  $A_1$ ,  $A_2$ ,  $A_1B$  and  $A_2B$ —are probably significant in causing some post-transfusion reactions, but direct support of this possible mechanism was lacking until Wiener's<sup>21</sup> report appeared last June.

Wiener has thoroughly analyzed a case of isoimmunization of an  $A_2$  recipient by transfusion of  $A_1$  blood. The  $\alpha_1$  behaved like a "cold" agglutinin. In another case,  $\alpha_1$  antibody was considered to have developed in an  $A_2$  woman as a result of isoimmunization by an  $A_1$  fetus in utero, the general explanation first proffered by Levine and Stetson<sup>5</sup> as the mechanism of reactions following primary intragroup transfusions given intra partum or post partum.

Since these are the only cases of this kind on record, it is clear that these subgroups play a very minor role in transfusion reactions. This is because the vast majority of bloods of Groups A and AB contain neither  $\alpha_1$  nor  $\alpha_2$ , and when present the latter are of low potency and are mostly active at low temperature. It seems likely that  $A_1$  and  $A_2$  are feeble isoantigens and produce immune isoantibody only in the rare persons who have some preformed  $\alpha_1$  or  $\alpha_2$ . The observations add to the evidence that the difference between  $A_1$  and  $A_2$  is qualitative. Although dangerous reactions are not likely to occur, it is desirable to use donors of homologous subgroups, that inapparent hemolysis may not deprive the recipient of the benefit of his transfusion.

The formation of anti-O isoagglutinin (probably the same as  $\alpha_2$ ) in low titer has been observed in a Group  $A_1B$  patient.<sup>24</sup> The transfused O cells disappeared rapidly from circulation, although the second transfusion of 300 cc. of O blood produced no symptoms.

#### TYPE-SUBSTANCES M, N AND P AS ISOANTIGENS

Normal isoantibodies for N have never been found; in only 4 cases among several hundreds of thousands of individuals tested has anti-M been detected.<sup>21, 25</sup> Although these three substances, especially M and N, are definitely antigenic in rabbits and other animals, they do not appear to incite the formation of antibody in man. With the exception of a single unconvincing report by Martinet,<sup>27</sup> Type N blood injected into Type M persons, or vice versa, does not produce type-specific isoantibody. Regarding substance P, for which it is difficult to produce immune serums in rabbits, one case is recorded<sup>4</sup> in which an intragroup



(A) transfusion resulted in the development of agglutinins for the donor's blood and for many others of Group A. Further tests revealed that agglutinin P was specifically affected by this isoantibody.

#### RH AS AN ISOANTIGEN

Last year, Landsteiner and Wiener<sup>28</sup> described an additional agglutinable substance in human blood that was recognized by its reactions with antiserum to rhesus (*Macaca mulatta*?) blood (hence termed "Rh"). This substance is common, being present in about 85 per cent of the population. Shortly after this discovery, Wiener and Peters<sup>4</sup> studied the bloods of 3 patients who had had hemolytic reactions, one fatal, after repeated transfusions of correctly grouped blood. The serums of these patients contained abnormal isoagglutinins reacting independently of the regular groups and corresponding to the property Rh, their blood cells did not contain Rh. Thus, the conditions for isoimmunization were present. The authors summarize their second case, in the light of the serologic findings, as follows:

A patient, group A (Rh-) was given a series of blood transfusions from two donors: one group A (Rh+), the other group A (Rh-). The first transfusion from the donor A (Rh+) gave rise only to a subclinical reaction. The following two transfusions from donor A (Rh-) were perfectly compatible so that the donor's cells could be demonstrated in the circulation of the patient (with the aid of the M-N test) for a long time afterwards. On the other hand, the blood from the first transfusion was gradually hemolyzed and eliminated, this being accompanied by the appearance of Rh antibodies in the patient's plasma. Later, when a second transfusion of blood from the first donor, A (Rh+), was given a hemolytic reaction followed. The long interval between the two transfusions from this donor probably allowed time for a fall in the titer of the anti Rh agglutinins so that these were not demonstrable either by the hanging drop or centrifuge technique before the last transfusion. The reason why the Rh agglutinins were not demonstrable immediately after transfusion is that they had been completely absorbed by the Rh+ blood introduced into the recipient's circulation. By the fourth day however, the antibodies had reformed in sufficient amount to be detectable.

Rh+ persons, being about six times as common as Rh-, are that much likelier to serve as donors. The conditions offering an opportunity for isoimmunization would obviously be the transfusion of Rh+ blood into an Rh- recipient. Such transfusions, if primary, would not be expected to result in reactions because normal anti Rh, which might be present in Rh- persons, has not been found, so, as with M and N, the factor Rh can ordinarily be disregarded in the selection of donors for primary transfusions. But an important ex-

ception must be well noted. The intragroup reaction reported by Levine and Stetson<sup>29</sup> led them to suggest the ingenious explanation that the fetus in utero is the source of an antigen, foreign to the mother, that gives rise to the production of an isoantibody capable of mediating a reaction to a transfusion of unsuitable blood given during or shortly after pregnancy. In these cases, as well as in repeatedly transfused patients, it has almost invariably been found by Wiener, Levine and their co-workers that the substance Rh is the antigen responsible, the reacting subjects being Rh-.

In such a pregnancy, the usual conditions are that the woman is Rh-, the husband Rh+, and the fetus has inherited the Rh factor from its father. During pregnancy, some Rh antigen from fetal blood (it appears to be absent from other tissues<sup>29</sup>) reaches the maternal circulation from time to time, perhaps through some placental defect, and incites the production of anti Rh. If the need for transfusion arises, the husband is often selected as donor, he is Rh+ (as are 85 per cent of donors, on the average), and the stage is accordingly set for a hemolytic reaction, which may be fatal. Cross matching of the bloods by the usual technique may not reveal the incompatibility, and even with the more delicate methods to be described, agglutination may escape detection.<sup>30</sup> Obviously, under these circumstances, and, in general, when one is dealing with patients who have received repeated transfusions, it is prudent to use Rh- donors.

#### ERYTHROBLASTOSIS FOETALIS

Strong corroborative evidence that Rh is an isoantigen of great clinical significance has been furnished by Levine and his collaborators. Levine and Katzin<sup>31</sup> observed that intragroup post transfusion reactions connected with pregnancy occurred especially in women whose obstetric histories disclosed an unusually high frequency of toxemias, miscarriages and stillbirths. Are these accidents correlated with the presence of irregular antibodies? Studies of erythroblastosis foetalis by Levine, Katzin and Burnham<sup>32</sup> furnished support for this speculation, 6 of 7 mothers possessed irregular agglutinin corresponding in specificity to anti Rh. Thus, the pathogenesis of the disease depends on isoimmunization of the mother against blood factors of fetal derivation and the subsequent transplacental passage of the maternal isoantibodies that cause destruction of fetal blood, accompanied by compensatory hematopoiesis.

The predominant role of the Rh antigen is shown in Table 1, which reveals an extraordinarily

high incidence of Rh- in the group of selected mothers, and of Rh+ among the husbands and affected children in these families.<sup>32</sup>

Further evidence of the correctness of the explanation proposed is that a large proportion of the mothers of erythroblastotic infants possess anti-Rh of sufficient strength to be demonstrable *in vitro*. The proportion diminishes with the lapse

TABLE 1. *Tests Made with Human Anti-Rh Serums.*

SUBJECTS	Rht +	Rht -
	%	%
1035 persons (general population)	86	14
153 mothers of infants with erythroblastosis	8	92
89 husbands of Rh- mothers	100	0
76 infants with erythroblastosis	99	1

of time after pregnancy—that is, as the period of antigenic stimulation becomes more remote.<sup>29</sup>

In some families, all pregnancies, except perhaps the first, yield infants with erythroblastosis; in others, some of the offspring are normal. Genetically, this difference could depend on whether the Rh property of the father is homozygous or heterozygous. According to Landsteiner and Wiener,<sup>33</sup> the property is inherited as a mendelian dominant and its absence is recessive.\* Half the offspring of a heterozygous (Rh+, Rh-) father would be Rh- and thus incapable of immunizing the mother, but if he is homozygous (Rh+, Rh+), all pregnancies will afford an opportunity for the production of anti-Rh. If the first infant is unaffected, it may be because a single pregnancy sometimes does not afford a sufficient stimulus for adequate immunization. Doubtless, mothers as well as transfused patients vary a great deal in the degree of their isoimmunizability as well as in its selectiveness, as the response of animals to heteroantigens does.<sup>36</sup>

Rh- blood is better for transfusing erythroblastotic infants<sup>29, 35</sup>; however, the mother's blood should not be used, since it probably contains anti-Rh. Theoretically, the mother's colostrum might contain a relatively high concentration of isoantibody; perhaps early nursing by the mother should be forbidden.<sup>37</sup>

To explain the few cases of erythroblastosis in Rh+ mothers, one may reasonably assume that

\*The hereditary nature of the Rh factor permits its use in cases of disputed parentage, but only when both mother and alleged father are Rh-, which occurs only once in forty nine times on the average, so that exclusions based on this factor are rare. However, one has already been found.<sup>34</sup> The putative father and the mother were Rh-, and the child was Rh+. Curiously, —a gross and shameful waste of exclusive evidence,—there was triple proof of nonpaternity (the falsely accused man belonged to Group B, the mother to Subgroup A<sub>2</sub>B, and the child to Subgroup A<sub>1</sub>B, furthermore, the man and woman were Type M and the child was MN).

Levine,<sup>38</sup> Javert<sup>39</sup> and Katzin<sup>40</sup> have found another atypical agglutinin in an Rh- mother of an erythroblastotic infant. It reacted mainly with a particular anti-Rh serum. Consequently, the substance detected by this agglutinin may perhaps be genetically related to Rh.

the same general mechanism is operating but that a different isoantigen is concerned. Antigenic components other than those already mentioned are known to exist in the red cells, and there is no reason to think that still more may not be discovered in the future.

Concerning this particular isoimmunologic disease, such antigens should not be sought in other tissues or fluids if interpretation of past lessons is correct. An early hypothesis was that if a Group B or Group O mother was carrying a Group A child, the mother's  $\alpha$  antibody might penetrate the placenta and cause destruction of fetal erythrocytes.<sup>38</sup> However, it could not be shown that such incompatibilities bore any relation to the disease, and it is now known that in most persons the substances A and B are present not only in the erythrocytes but also in various tissue cells and that they are dissolved in various secretions, including the amniotic fluid. This wide distribution allows neutralization of the isoantibodies and serves to protect the fetal red cells. Possibly, those who do not secrete such substances would be less well protected.

An explanation offered by Darrow<sup>39</sup>—that icteric symptoms might be due to an isoimmunity involving differences between maternal and fetal hemoglobins—has not been substantiated. There is, however, a recent report<sup>40</sup> that such antigenic differences do exist and that fetal hemoglobin is more complex than the adult kind; that is, the precipitins in an antiserum for adult hemoglobin are completely absorbed by either antigen, but antiserum for fetal hemoglobin still reacts with the homologous antigen after the precipitins for adult hemoglobin have been completely removed.

#### EXTRACELLULAR ISOANTIGENS

There has long been considerable speculation<sup>41</sup> about the possibility that incompatibilities may not be restricted to differences between the cellular elements of the blood and the corresponding iso-hemagglutinins or lysins. A few observations suggest that there may be sufficient isoantigenic differences between the proteins of plasma so that, under appropriate conditions, isoprecipitins or sensitizing antibodies may be formed and may be instrumental in producing allergic shock. In 1916, Marie reported two cases of serum sickness in typhoid patients following a second injection of human serum from typhoid convalescents.<sup>41</sup> Urticarial reactions after transfusions have been described by many authors and are commoner and, usually, severer after repeated transfusions, especially if the same donor is used. Böttner<sup>42</sup> and Traut<sup>43</sup> have discussed this anaphylactic aspect

of the problem Gyorgy and Witebsky<sup>14</sup> observed a patient who, at intervals of several days, was given a transfusion from the father, a second from the mother, and a third from the father. Symptoms of severe shock after the third transfusion were relieved by epinephrin. The patient's skin reacted to the father's but not to the mother's serum, and the patient's serum fixed complement in the presence of the father's serum but not of the mother's. A similar case of selective cutaneous reactivity is reported by Wiener et al.<sup>14</sup>

#### TECHNICAL CONSIDERATIONS

From the foregoing review, it is obvious that unusually careful precautions must be taken when one is testing for compatibility prior to transfusing pregnant and recently delivered women or any patients who have received previous transfusions. Immune isoantibodies may remain in the circulation for only a few weeks<sup>7</sup> or for more than a year.<sup>29</sup> Wiener and Forer<sup>30</sup> give an example of how extremely complicated the selection of a compatible donor may be. A woman had had chills, fever and jaundice following two transfusions. She belonged to Group O, but her serum agglutinated the cells of each of 28 Group O persons tested. Besides the normal anti A and anti B in her serum, there were two abnormal agglutinins, anti Rh and anti M. The patient was Rh- and Type N, as would be expected. Inasmuch as one person in five is Type N and one in seven Rh-, it is to be expected that one in thirty-five persons will be N Rh-. Among 90 Group O donors tested, 2 were found to be ON Rh-. Their bloods did not cause any reaction when transfused into this patient, who entirely recovered.

The necessity of having highly potent serums available for purposes of grouping bloods has been sufficiently stressed.<sup>4,18</sup> It is also apparent that the so-called "universal" donor\* does not exist. Even an O Rh- blood containing weak  $\alpha$  and  $\beta$  antibodies cannot be safely used in the rare A and A<sub>1</sub>B recipients whose serums contain anti O ( $\alpha$ ). Considerable difficulty has been experienced in obtaining useful anti Rh serums, which have been derived from rabbits immunized with rhesus blood,<sup>28</sup> from human beings accidentally immunized,<sup>29</sup> and, very recently, from guinea pigs

injected with rhesus blood.<sup>33</sup> The specific reactivities of different serums are usually but not invariably parallel.<sup>43</sup> This complication may tentatively be ascribed to the existence of subgroups such as Rh<sub>1</sub> and Rh<sub>2</sub>. Anti Rh serums also differ in the thermal range of their activities. Some have the property of so-called "cold" and others of "warm" agglutinins. It would be safest to run tests in triplicate, one in the icebox, one at room temperature, and one at 37°C. For the last, thirty minutes' incubation followed by centrifugation for one minute at 500 r.p.m. is recommended. If, on resuspension of the sediment, no gross agglutination is apparent, the preparation should be examined microscopically.<sup>51</sup>

Technics and general precautions have recently been described in full.<sup>4,18</sup> Inasmuch as the irregular isoagglutinative reactions are much weaker in intensity than those produced by anti A and anti B or anti M and anti N, it is desirable to use the most sensitive technics possible. Lund's<sup>52</sup> experiments with the regular isogglutinins show that a noteworthy refinement can be achieved by diminishing the concentration of cells and increasing the quantity of serum used in the test, thus allowing more antibody for each erythrocyte. The usual concentration of cells recommended, 1 to 2 per cent, was found to be excessive and relatively insensitive. A concentration of about 0.06 per cent was eight times as sensitive as one of 0.5 or 10 per cent. Concentrations less than 0.007 per cent were thirty-two times as sensitive. Use of these low concentrations involves centrifugation and secondary reduction of the volume of supernatant to secure a suitably dense suspension for microscopic examination.

The quality of agglutination in the Rh system is peculiar, being reminiscent of the floccular rather than the granular type observed in bacterial agglutination. Wiener<sup>37</sup> thinks that the Rh antigen may be located partly below the surface of the cell whereas A, B, M and N are superficially located antigens. A new so-called "sedimentative" technic has just been described by Landsteiner and Wiener.<sup>33</sup> Because of the importance of the Rh antigen and the need of further work designed to facilitate its detection, this procedure is described in full.

For the production of the sera large guinea pigs were injected intraperitoneally with a suspension of washed red cells of rhesus monkeys, each animal receiving a dose corresponding to 1 cc. in later experiments to 2 cc. of whole blood. The injection was repeated after five days, and one week later the animals were bled. The sera of the majority of animals were found to show a difference between the two sorts of blood, Rh+ and Rh-, and in a group of ten animals

\*A method of rendering human donors blood serifer by neutralization of  $\alpha$  and  $\beta$  has been proposed by Wiener and Landsteiner.<sup>34</sup> The addition of a few ml. of the oil of A and B still leaves 500 cc. of supernatant blood sufficient to reduce the agglutinating capacity to very low levels. This is satisfactory altogether. These workers state that 0.5 or 100 ml. of neutralized Group O blood have been given mainly to patients belonging to the other three groups with satisfactory clinical results. A few cross reactions were sometimes met with. If the expense of isolating the group substances is not too great, this method may have some usefulness, but it does not remove the need for careful precautions in the serum transfusions chiefly discussed in the present review, and it does not reduce the danger of transfusing Group O blood into the occasional recipient of Group A or A<sub>1</sub>B who has anti O agglutinins.

usually one or more were found that yielded sera suitable for practical diagnosis. The manner of selecting the sera is given below.

While in the case of the immune rabbit sera the reagent was prepared in the customary way by absorbing the diluted serum with negatively reacting blood, it was found with several guinea pig sera that absorption with human blood resulted merely in a non-specific diminution of the agglutinin content, no matter whether positive or negative blood was used. This led us to test the effect of simple dilution, and indeed it was found that a distinction between positive and negative bloods could be made directly without absorbing sera. (As an analogy, mention may be made of rabbit immune anti-A sera which cannot be specifically absorbed with A<sub>2</sub> cells to produce a reagent for A<sub>1</sub>, absorption with A<sub>2</sub> blood serving merely to diminish the agglutinin titer.)

The method for determining suitable sera consists in making serial dilutions by halves and testing with known negative and positive blood. Those sera which show in three (or more) successive dilutions negative reactions with the former and positive ones with the latter blood are usable.

The actual tests can usually be carried out simply by selecting a dilution of the serum, e.g., 1:10, which gives no reactions with negative but definite reactions with positive bloods, those sera that contain appreciable amounts of anti-A or anti-B agglutinins having been

to 1 hour, by direct inspection of the bases of the tubes, with a hand lens. Negatively reacting bloods then show a circular deposit with a smooth edge, while positive bloods have a wrinkled sediment with a serrated border or show a granular deposit [Fig. 1]. From these readings, as a rule, the diagnosis can readily be made. The readings are facilitated by using racks having small holes beneath the bottom of the tubes. Following the reading the tubes are shaken and the sediment examined after it forms again. A further examination is made after 2 hours, again inspecting the sediment. The tubes are then gently shaken and the suspension is examined microscopically: the negative blood samples are mostly perfectly homogeneous; the positive ones show various degrees of agglutination, not infrequently visible to the naked eye. At times, the clumping is quite weak in spite of a distinctly positive sediment picture. Needless to say, positive and negative control bloods should be included in each test.

As already mentioned, with the great majority of specimens the distinction between positive and negative reactions is quite definite but the positive reactions vary in strength and some bloods offer difficulties because of their weak reactions. However, after sufficient practice, and by repeating the tests if necessary with fresh blood samples and several sera, only in some few instances were the reactions questionable. Marked differences in the intensity of the reactions were also observed in tests made with human anti-Rh sera.

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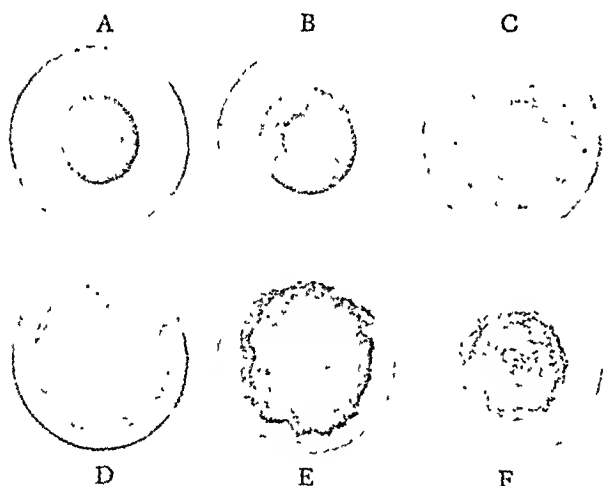


FIGURE 1. Appearance of Sediments in Bottoms of Tubes. (Reproduced from Landsteiner and Wiener<sup>33</sup> with permission of the publisher.)

A and B are negative reactions, the inner light disk of the latter being due to a slight convexity in the bottom of the tube; C is a faintly positive reaction; D is a weak reaction; E and F are positive reactions.

previously absorbed with small quantities of A and B blood. Since the sera are used diluted, inactivation is mostly unnecessary. The blood to be tested should be fresh.

Another method, alternative to dilution alone, is to absorb the sera diluted, e.g., 1:4 with a quantity of blood (using A or B cells if indicated) sufficient to remove the reaction with Rh-negative blood.

Two drops (0.1 cc.) of the test fluid are then mixed with one drop of 2 per cent (in terms of blood sediment) washed blood suspension, freshly prepared, in a narrow tube of 7 mm. diameter and allowed to stand at room temperature. Readings are taken after sedimentation has occurred, usually after 30 minutes

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 27481

#### PRESENTATION OF CASE

A fifty-three-year-old housewife was admitted to the hospital because of jaundice, dark urine and light stools.

About six months before entry, the patient noted the gradual onset of a feeling of "exhaustion," which persisted. Previously, she had been in good health. At about this time, following a "bad cold," she noticed a yellowish tint to the skin. She then began to have from three to five loose bowel movements each day; no blood was passed, however. The patient gradually lost appetite. About seven or eight weeks before entry, there was occasional nausea and vomiting of yellowish material. About a week later, she noticed that her urine became darker and her stools became "putty-like." Her former diarrhea had been replaced by constipation. At about this time, she noted that her skin had again become yellow. From then on, the jaundice continued to deepen. Once, while vomiting, the patient put her hand on the upper part of her abdomen, and became aware of tenderness toward the right side. There was, however, no spontaneous pain until the last few days before entry, when there was a dull ache in the back over the spine of the right scapula. About a week before entry, the patient had some sweating at night, associated with bitemporal headache. She had no chills. On one occasion her temperature was 102°F.

The family and past histories were not of importance. A year before admission to the hospital, a boy boarding at the patient's house developed typhoid fever. Specimens of the patient's blood, urine and stools were therefore examined by the State Laboratory. She was found to be a typhoid carrier, and was obliged to give up her boarding clients.

On admission, the patient was very obese, but was in no acute distress. The skin and scleras were moderately jaundiced. The heart and lungs were not remarkable. The abdomen was obese, with voluntary spasm and tenderness to deep pressure over the upper portion, more marked toward the right. A poorly defined mass was palpable in the right upper quadrant.

The temperature was 101°F., the pulse 95, and the respirations 22. The blood pressure was 96 systolic, 50 diastolic.

Examination of the blood showed a red-cell count of 5,520,000, and a white-cell count of 9200 with 82 per cent polymorphonuclears. The serum contained 9.6 mg. bilirubin per 100 cc., with a diphasic van den Bergh reaction. The serum protein was 6.6 gm. per 100 cc. The prothrombin time was 31 seconds (against a normal of 22 seconds). The hematocrit was 46.8 per cent. The blood Hinton reaction was negative.

The urine showed a ++ test for albumin, with occasional clumps of red and white cells in the bile-stained sediment; it was sterile on culture. The stools showed no pathogens in five successive cultures; on one occasion, an "atypical" colon bacillus was isolated.

The patient was given repeated venoclyses of glucose solution. After the first few days, her temperature remained normal. On the twelfth hospital day, duodenal drainage yielded a small amount of fluid with a bulky sediment that contained numerous red blood cells, occasional clumps of white blood cells and occasional clumps of calcium bilirubinate crystals. There were no cholesterol crystals.

On the thirteenth hospital day, an operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR. WYMAN RICHARDSON: "She noticed a yellowish tint to the skin." This is important. The question is whether or not there was real jaundice at this time. As we know, patients frequently complain of a yellowish tint that is not due to jaundice. However, in view of the fact that the patient did develop jaundice later, it is perhaps significant in this story.

I might say that I do not see why an operation was performed on this patient in the light of the evidence given here. Realizing that it is very difficult to make these summaries in a brief form, however, I should like to say that one of the easiest tests to perform is that of looking at a stool. As a matter of fact, such a test is one of the hardest things to get done in a hospital. These stools were all sent off and cultured. Whether anyone looked at them, I do not know. I should like very much to know whether the stools were brown or gray.

DR. TRACY B. MALLORY: It is reported that the stools were tan colored.

DR. RICHARDSON: That means to me that some bile was getting through the gastrointestinal tract.

One other thing about the operation: in these

exercises, an operation sometimes includes a peritoneoscopy, so that this patient was not necessarily operated on with the idea of some very radical procedure.

The first question to decide, if possible, is, of course, whether a case of this sort represents intrahepatic disease or an obstruction of the major bile ducts. I believe that the evidence is more in favor of intrahepatic disease than of biliary obstruction. If this had been a case of tumor located at the ampulla or thereabouts, one would expect a progressive increase in the jaundice, which might wax and wane but which should, on the whole, be progressive. Obstruction characteristically produces a severe jaundice frequently associated with severe itching. This jaundice was described by the examiner as moderate, and the van den Bergh reaction corroborates the fact that, although fairly marked, it was not the very severe type that would be seen in complete biliary obstruction. Furthermore, obstruction of the bile ducts by tumor is rarely associated with a febrile reaction, so that I do not believe that this patient had tumor of the biliary tract.

Infection of the biliary tract might account for the fever this patient had; it was not typical of cholangitis, however. A Charcot fever is often associated with real chills. Usually, it runs a short course, and one would not expect it to be relieved by intravenous glucose. That last statement, however, may not be true: the subsidence of fever may not have been due to the administration of glucose; it may have been a coincidence.

The problem of the mass in the right upper quadrant comes into the picture at this point. The abdomen was obese, and the mass poorly defined. Taking these two statements together, in discussing this case, I shall have to assume that there was no mass. The examiner seems not to have been very certain of it. If there was a definite mass, the examiner might have thought that it represented the gall bladder, and an enlarged gall bladder would be, perhaps, slight evidence against the presence of gallstones, according to Courvoisier's law, although that does not hold very much more often than in half the cases. The mass, if there was a mass, might represent some form of tumor in that region and might lend weight to a diagnosis of neoplastic disease. On the whole, the evidence is against an obstruction of the biliary tract, especially low down.

I want to bring up three possibilities, which I wish to discard. The first is the question whether this patient might have had ulcerative colitis, accounting for the diarrhea, because we have seen

some patients with ulcerative colitis who developed degenerative liver disease. The cases that I have seen have occurred in patients who had very severe ulcerative colitis and obviously were very ill, whereas this patient, if she had ulcerative colitis, was not sufficiently sick to lead anyone to suspect it and to look for it; so that I think such a diagnosis is unlikely. The question of amebic dysentery comes to mind because of diarrhea and fever, and I wonder if amebic abscesses could produce this degree of jaundice. I think that perhaps they might, but I do not quite see how they could unless there was very extensive disease of the liver. We might just as well rule that out. There is no way of proving it unless the amebas were discovered, and I assumed that they were not looked for. Finally, what bearing did the typhoid bacillus in the biliary tract have on this patient's illness? I must confess that my knowledge of typhoid infection is very slight. Back in 1923, at the time of my first contact with this hospital, we saw four or five cases of typhoid fever during a period of service. I do not recall seeing a case for the past five years. However, if a patient is living with the typhoid bacillus in the biliary tract he would be less likely to have generalized infection as a result of it, having acquired this symbiotic relation. Whether the presence of these bacilli is likely to result in the formation of stones, I am not certain, in spite of the textbooks. On the whole, I believe that the presence of the typhoid bacillus and the fact that the patient was a carrier are probably red herrings in this case.

So far as cholangitis is concerned, I have never been quite sure what cholangitis represents. I gather that it is an infection of the biliary tract that results in jaundice and infection, may be associated with small abscesses in the liver, and may eventually result in a biliary cirrhosis, if the patient does not die first. One should consider cholangitis in this case, but I do not see any suggestion of cholangitis unless we assume that there was obstruction, possibly due to stone, which I have been inclined to rule out. Acute cholecystitis might have been considered, but we must account for jaundice by an acute empyema or infection of the gall bladder. If that were so, we should have to assume that the patient had a stone in the common duct as well as in the cystic duct. Furthermore, I again bring up the fact that the fever apparently subsided after intravenous glucose therapy.

Then, the question of an intrahepatic disease comes up, and I briefly note the patient's symp-

toms. She had a feeling of exhaustion and what was called a cold. She had some apparent infection, followed by diarrhea, then jaundice and fever, with very little pain. It seems to me, taking the whole picture together, that the most likely diagnosis is a toxic hepatitis, with some degeneration or even destruction of the liver associated with fever; when treated in the hospital with glucose, the process might have been held in abeyance.

I should like to emphasize one other point: the blood smear. The patient had a white-cell count of 9000, with 82 per cent polymorphonuclears; this would be consistent with some sort of infection. There was apparently a reduced number of lymphocytes—they must have been less than 18 per cent. If monocytes had been present, there might have been less than 10 per cent, and reduction of lymphocytes could be associated with some lymphoid tumor: lymphoma or Hodgkin's disease of some type. I consider that poor evidence to bring up in favor of lymphoma.

The decision what to do with a patient with jaundice often depends on the course. Here again, I have a right to be a little "peevish" because I do not know the course during the twelve days under treatment, but one gets the impression that the patient was improved. We know that the temperature came down. We do not know whether the jaundice decreased or remained the same. Duodenal drainage was done, but the color of the aspirated fluid is doubtful. I do not know whether calcium bilirubinate crystals are sufficient to give bile color, and shall not take the time to talk about it. I do not consider it important because we have the stool examination. The finding of cholesterol crystals in the bile or the finding of a considerable amount of cholesterol crystals in the duodenal drainage has been considered evidence of gallstones. I am not sure that calcium bilirubinate crystals have the same significance, and on the whole I discard that finding.

To summarize, it seems to me that the course of this disease is that of a toxic hepatitis. I believe that this progressed to a serious degree of actual liver degeneration, and that when this patient was operated on some evidence of a toxic cirrhosis or fibrosis of the liver was found. The operation, I hope, was a peritoneoscopy, because that procedure, in my opinion, might have made a radical operation unnecessary. It is only fair to say that I should assume that the patient, before being operated on radically, would have had more study of the gastrointestinal tract by x-ray or otherwise. She may have been under mosquito bars, and they may not have wanted to take her down to the x-ray room. One other thing: it is true that cholecystectomy has often resulted in the

elimination of typhoid bacilli from the stools of carriers, but I assume that this patient was much too sick for operation, on that basis, to be considered.

A PHYSICIAN: How do you explain the blood in the duodenal drainage?

DR. RICHARDSON: I might have mentioned that; I considered it quite carefully. One can find numerous red cells from the trauma of passing the tube. We frequently get positive guaiac tests following gastric analysis without a lesion, and therefore I did not believe that one need account for red cells on the basis of an ulcerative lesion. There may have been a bleeding tendency because of a slightly increased prothrombin time.

DR. ALLEN G. BRAILEY: A toxic hepatitis might perfectly well have followed a stone in the common duct with partial obstruction.

DR. MURRAY COPELAND: I have seen jaundice in association with cholecystitis and no stone.

DR. RICHARDSON: Due to cholangitis, I suppose.

#### CLINICAL DIAGNOSES

Obstructive jaundice.

Typhoid cholecystitis.

#### DR. RICHARDSON'S DIAGNOSIS

Toxic hepatitis, with secondary cirrhosis of the liver.

#### ANATOMICAL DIAGNOSES

Colloid carcinoma of gall bladder, with direct extension to common and cystic bile ducts, liver and pancreas, and with metastases to peritoneum, ovary, mesenteric and retroperitoneal lymph nodes, mediastinum, kidneys, lung, liver, pleura and thoracic duct.

Icterus.

Ascites.

Hydrothorax, slight.

Chronic vascular nephritis, slight.

Endometrial polyp.

Obesity.

#### PATHOLOGICAL DISCUSSION

DR. MALLORY: I think one's attitude to the case must depend on how seriously one takes the mass in the right upper quadrant, which certainly was not described in the record as anything very distinct. I gather, however, that the surgeon in charge of the case believed more strongly that there was a mass. At any rate, he decided on an exploratory operation, with the diagnosis of obstruction to the common duct. He did not commit himself as to whether it was due to stone or neoplasm. The abdomen was opened, and an enlarged gall bladder, with walls that were ex-



remely thick and very hard, was found. In spite of prolonged efforts, the surgeon, and he was a competent one, was unable to locate the common duct. He took a piece of tissue from the wall of the gall bladder and backed out. He also aspirated the gall bladder. It contained some colorless fluid, which was sent to the laboratory for culture. The liver appeared grossly normal except for slight enlargement and bile staining. The patient then pursued a rather rapid downhill course and died in approximately three weeks. The biopsy showed carcinoma of the colloid type and at autopsy we found a cancer involving the gall bladder, the extrahepatic and intrahepatic bile ducts and the region of the head of the pancreas. In cases such as this, it is sometimes quite difficult to decide at autopsy where the cancer is primary. The possible foci are the gall bladder itself, the bile ducts and the pancreas. In this case, it seemed quite obvious that the pancreas was secondarily involved. The bile ducts, although completely surrounded by tumor and constricted by external pressure, were not invaded or actually occluded, so that I think we can be fairly confident that this tumor was primary in the gall bladder.

Culture of the gall bladder at the time of autopsy gave a pure culture of typhoid bacillus. Cancer of the gall bladder, we know, almost invariably occurs in patients who have been chronic carriers of gallstones for ten to twenty years. It is the greatest danger of the so-called "silent stone" in the gall bladder. We were therefore surprised to find no gallstones in this case. On the other hand, we have reason to believe that this patient had had a very chronic cholecystitis for many years, owing to the presence of the typhoid organisms. It is at least possible that a typhoid cholecystitis was the long-standing focus of chronic inflammation on which this neoplasm developed. That would be my final interpretation of the case. There was a very slight degree of cholangitis, but the major functional lesion was carcinomatous infiltration around the bile ducts. There were peritoneal implants and also numerous distant metastases.

DR. RICHARDSON: Was any bile getting through?

DR. MALLORY: Bile was still coming down from the liver. It obviously was not passing through the cystic duct, since the bile in the gall bladder was perfectly colorless; however, the bile in the common bile duct and in the hepatic ducts was orange.

For about two years, the patient had suffered from "gallstones," occasionally associated with attacks of colic, and at times with jaundice. On the morning before entry, she did not feel well and soon after eating a piece of candy developed an acute, very severe, right-upper-quadrant pain, which tended to travel "down." A few hours later, she began to vomit, and continued to vomit frequently during the night. The pain was intermittent and, despite medication by her physician, persisted until entry.

Thirteen years before entry, both breasts had been removed for cystic disease, and three years later, an operation on the uterus was performed.

Physical examination showed a well developed and well-nourished, acutely ill woman, who was heavily narcotized. The lips and fingers were cyanotic. There was no icterus. Examination of the chest was negative. The abdomen was moderately distended. There was extreme tenderness, with resistance, across the upper abdomen, and distinct spasm in the right upper quadrant. No masses or organs could be palpated. There was some tenderness below the right costal margin posteriorly and in the right lower quadrant, but it was not so marked as that in the upper abdomen. Peristalsis was heard on only one examination, when there was an occasional rush associated with pain.

The temperature was 99°F, the pulse 105, and the respirations 28. The blood pressure was 120 systolic, 90 diastolic.

Examination of the urine showed a large trace of albumin, a green reaction to Benedict's test and 2 or 3 white cells, many hyaline and granular casts and a few cellular casts per high power field. The blood showed a red-cell count of 5,100,000 with 86 per cent hemoglobin, and a white-cell count of 10,000. A few hours later, the white-cell count was 6000 with 69 per cent polymorphonuclears. There was a decided polymorphonuclear shift to the left, the majority of the neutrophils being young forms with single lobes.

X-ray study of the abdomen showed no evidence of free gas beneath the diaphragm. There was a large amount of gas in the colon and small bowel, but no definitely dilated loops were seen.

The patient's condition rapidly became worse, the temperature rising within a few hours to 103°F. and the pulse to 150. She died nineteen hours after entry.

#### DIFFERENTIAL DIAGNOSIS

DR. RICHARD WARREN: This elderly woman died within forty-eight hours of the onset of an attack of abdominal pain which was so severe that it was uncontrollable by several doses of morphine. This pain was due to some "peritoneal insult" in

#### CASE 27482

##### PRESENTATION OF CASE

A sixty-eight-year-old housewife was admitted in a semistuporous, moribund condition

the upper abdomen, more on the right side than elsewhere. None of the available information is revealing enough to allow me to make a diagnosis that I am confident is correct. Several possible diagnoses suggest themselves, and from these I shall select the one that seems to me the most probable.

The commonest cause of such severe, sudden upper abdominal pain is a perforation of the stomach or duodenum from either ulcer or cancer. There is no history of ulcer or cancer, however (unless one accepts the "gallstone" story as perhaps indicative of one of these), and no subphrenic air was seen by x-ray examination. Moreover, the patient died more rapidly after onset than the usual patient with untreated gastroduodenal perforation.

It is quite certain from the history that the patient had gallstones. The association of jaundice with the attacks of pain supports this very strongly. It is tempting, then, to assume that the terminal episode in the case was some complication of cholelithiasis. The two complications that could give this picture are acute cholecystitis, with perforation, and acute pancreatitis. The former rarely perforates so early in the attack as this, even if complicated by carcinoma of the gall bladder, and is rarely so fulminating. Acute hemorrhagic pancreatitis is a distinct probability. The extreme tenderness across the upper abdomen, the persistent vomiting, the failure of the pain to respond to morphine, the suggestion of tenderness posteriorly and the rapid downhill course all suggest this diagnosis. One would like to see tenderness extending more toward the left upper quadrant than toward the right lower quadrant, but that is not essential.

The only other diagnosis that seems likely is infarction of some intraperitoneal organ, specifically a loop of small intestine. The previous abdominal operation, the abdominal distention, the normal temperature and rising pulse when first seen and, most particularly, the fact that an occasional rush of peristalsis was associated with pain are in favor of this. Against it, however, are the presence of gas in the colon by x-ray examination, and of maximum signs in the upper abdomen at some distance from the abdominal scar and the fact that the physicians in charge did not consider this diagnosis seriously enough to operate.

The only point in the case that makes one somewhat suspicious that the sole diagnosis was pancreatitis is the fact that at two places in the case summary it is intimated that the process tended to

spread to the right lower quadrant. This suggests a leak of some septic or irritating fluid down the right gutter. This is possible in pancreatitis, and may represent fat necrosis. It would, however, be more likely in duodenal or cholecystic perforation.

#### CLINICAL DIAGNOSES

Perforation of gall bladder.  
Peritonitis.  
Acute cholecystitis.

#### DR. WARREN'S DIAGNOSES

Cholelithiasis.  
Acute hemorrhagic pancreatitis?  
Perforation of the gall bladder?

#### ANATOMICAL DIAGNOSES

Acute hemorrhagic pancreatitis.  
Acute aseptic peritonitis.  
Multiple fat necroses.  
Bronchopneumonia.  
Cholecystitis, chronic.  
Cholelithiasis.  
Operative scars: bilateral simple mastectomy; appendectomy; ventral suspension of uterus.

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: Dr. Warren was able quickly to narrow down the differential diagnosis to two possibilities: perforation of the gall bladder and acute hemorrhagic pancreatitis. It is evident that the clinicians on the ward also went through an essentially similar process of reasoning, but as their first choice they picked perforation of the gall bladder. The post-mortem examination proved that Dr. Warren was correct. When the abdominal cavity was opened, considerable amounts of slightly turbid fluid were found in which were numerous droplets of fluid fat. All the peritoneal surfaces were studded with small chalky foci. When the gastrocolic ligament was incised, the anterior surface of the pancreas presented as a swollen, purplish mass. Incision into the organ demonstrated many spots of chalky fat necrosis and also many semiliquid foci of hemorrhagic necrosis. As is almost always so in hemorrhagic pancreatitis, there was a diseased gall bladder. Its walls showed fibrous thickening. It contained turbid fluid with but little color and eighteen small, rather friable gallstones. The hepatic and common bile ducts were normal, and there was no stone at the ampulla. The remainder of the autopsy showed little of interest. There was minimal aortic and coronary sclerosis and bare traces of incipient bronchopneumonia.

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## HIDDEN HUNGER

Mass starvation requires time before its full impact is felt. The past winter in Europe, devastating as it must have been, did not produce the degree of physical injury that was feared. Populations might have been in the process of starving, but they had not starved; the fatted calves had been rerouted into Germany, but bellies could still be filled with the husks that the swine had left; epidemics of disease were anticipated, but they did not materialize.

Dr. Harold C. Stuart, of the Harvard School of Public Health, recently spoke to the American Academy of Pediatrics concerning some of his observations in visiting unoccupied France this year. The people there, and particularly the chil-

dren, were not, apparently, so poorly nourished as had been expected; certainly, they were in much better condition than those of Spain, through which country the party had traveled into France. However, in those cases in which vitamin levels of the blood were determined, the significant fact was brought out that these levels were low, occasionally to the point of depletion.

At the same meeting, Surgeon General Thomas Parran, of the United States Public Health Service, elaborated on the distinction between the "hollow hunger" of empty starvation and the "hidden hunger" of vitamin, mineral and protein deficiency. Hollow hunger can be mitigated from time to time by the husks of food with which the belly may be filled; hidden hunger gnaws relentlessly on, sapping the strength, the vitality and the ambition of its victims.

Hidden hunger is the inexpensive, scientific weapon with which Germany can and will hold whole nations in subjection once they have been conquered by the sword. An adequate diet is the weapon with which we, as a nonbelligerent (if not a silent) partner, must make sure that we adequately equip our allies. A country that a few short years ago was ploughing under its wheat, burning its potatoes and killing off its hogs may soon be forced to step up its production and even ration such critically important food supplies as meat, cheese, eggs and milk, that the unconquered democratic countries may maintain their vigor, their initiative and their resistance.

This task and this sacrifice are up to us. We are still living in a land of plenty, but we may yet have to tighten our belts if those nations with which we have thrown in our lot are to achieve eventual victory, or even, perhaps, remain unconquered.

## GOLDEN JUBILEE

ANOTHER milestone in the progress of "quality-milk" production was passed when, on September 17, the Walker-Gordon Farm at Charles River Village, Massachusetts, celebrated its fiftieth an-

niversary. At that time, the World's Fair rotolactor was officially dedicated. A few weeks later, the fiftieth anniversary was further celebrated at the Walker-Gordon Farm at Plainsboro, New Jersey, where the original rotolactor has been in service for several years.

Although certified milk and Walker-Gordon have been associated in our minds for years, so that the terms have seemed almost interchangeable, the two developments, directed toward the same purpose, appeared spontaneously and independently. Walker-Gordon started producing what was probably the world's first really clean milk in 1891 in Massachusetts; Dr. Henry L. Coit, of Newark, New Jersey, conceived the idea of the medical certification of certain dairy farms in 1893, and, the first farm to be so certified was in that state.

The certification of farms physically equipped to produce pure milk and managed by farmers intellectually and morally equipped for its production has been the most powerful motivating force for improvement that the milk industry has ever received. Today, however, certification or noncertification is not so important as the facts that knowledge of the requirements of clean milk production are well known, the way having been shown by certified milk, and that, by and large, the certified farms still fulfill these requirements.

Walker-Gordon Farm, which antedates certification, has long served as a model certified dairy, as well as a research laboratory for the scientific improvement of milk production and the modification of milk for infant feeding. Here, vitamin D milk was first produced on a commercial scale, and many improved methods of laboratory control were developed; at the Plainsboro farm, the forage dehydrator, a conserver of vitamin A, first came into use.

The installation of the rotolactor, making a complete inexorable revolution every ten minutes, with its constant procession of disciplined mammals, furnishes a token that Walker-Gordon is looking forward to another fifty years of progress. Six prize bulls, serving numbers of selected cows by artificial insemination, are a guarantee that good milking stock will be perpetuated.

## MEDICAL EPONYM

### ISLANDS OF LANGERHANS

These structures are described in an inaugural dissertation submitted in candidacy for the degree of Doctor of Medicine from the Friedrich Wilhelm's University at Berlin on February 18, 1869, by Paul Langerhans (1849-1888), entitled "Beiträge zur mikroskopischen Anatomie der Bauchspeicheldrüse [Contributions to the Microscopic Anatomy of the Pancreas]." This monograph was privately printed by Gustav Lange, of Berlin, in 1869. A portion of the translation follows:

These cells are small and irregularly polygonal in form; their contents are quite homogeneous, glistening and without granules; the nuclei are clear, round and of medium size. Their average diameter is from 0.0096 to 0.0120 mm., and that of the nuclei from 0.0075 to 0.0080.

These cells for the most part lie in clumps, peculiarly distributed in the parenchyma of the gland. If a pancreas that has been in Müller's liquid for two or three days is examined under low power, such as No. 4 objective in Hartnack's system, there will be observed regularly scattered in the gland rounded spots stained a deep yellow, about one to a field when a No. 3 ocular is used. Under higher powers, it is evident that these spots consist entirely of our cells. They are heaped up in rounded clumps, regularly distributed in the parenchyma (in the old meaning of the word) of the gland. The clumps have for the most part a diameter of 0.10 to 0.24 mm., and can easily be perceived even in teased preparations made either from fresh glands or from those that have been treated for a short time with iodine serum.

R. W. B.

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

#### FATAL LOBAR PNEUMONIA IN PREGNANCY

A thirty-six-year-old primipara who had had no care whatever was seen, when about eight months pregnant, by her family physician, who immediately referred her to the hospital with a diagnosis of lobar pneumonia.

The temperature was 103°F., the pulse 130, and the respirations 32. Physical examination showed a well-developed woman. The heart was not enlarged; there were no murmurs. The entire left lung was consolidated. The pulse was rapid. The uterus was enlarged to a size consistent with an eight months' pregnancy. The general physical condition was very poor.

Two days after admission, the patient started in

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, Secretary, 330 Dartmouth Street, Boston.

labor and delivered herself spontaneously of a still born infant. She died the following day.

**Comment.** Pneumonia has always been recognized as a very serious complication of pregnancy. This death occurred before chemotherapy in pneumonia had been established, and although chemotherapy might have influenced this outcome, it is very doubtful whether the result would in any way have been changed after the patient was seen. This death can be attributed either to neglect or ignorance on the part of the patient. Why the patient had not consulted anyone is not clear from the record. Probably, her economic status had much to do with this, although prenatal clinics are available for those who cannot afford their own physician. It is essential that patients who are pregnant, particularly in the later months be warned about the seriousness of the common cold and that they be advised to have medical attendance immediately. In this way only may pneumonia sometimes be averted, and in this way only may chemotherapy be instituted soon enough to be of value.

As is very common in serious cases of pneumonia during pregnancy, this patient delivered herself spontaneously of a stillborn infant after a short labor. Recoveries do occur in some patients who seem desperately ill and whose uterus is spontaneously emptied, probably because the load on the heart is lessened and the lungs are given freer space for expansion. It is an obstetric axiom, however, that artificial induction should never be attempted.

## MISCELLANY

### PREVAILING INFECTION RATE OF TUBERCULOSIS

The mortality from tuberculosis has been quartered in forty years. This fact, however, reveals no accurate information regarding prevailing infection and morbidity rates. That they are less is too logical a deduction to be doubted but their decline relative to that in mortality has been a matter of conjecture. The following report on autopsy findings (Lande, K. E., and Wolff, G. Frequency of tuberculous lesions at autopsy *Am Rev Tuberc* 64:223-239, 1941) throws valuable light on this question especially since accurate studies extending over the past half century furnished the needed controls for comparison.

In 1900, Naegeli published a careful report of 508 autopsies. Of the adults over eighteen years of age 93 per cent showed healed inactive or active tuberculous lesions in the lungs. Only 17 per cent of those under eighteen yielded positive findings. Other investigators substantiated these findings, and in the early years of this century the belief was prevalent that all adults had at some time suffered an invasion by the tubercle bacillus.

Opie as late as 1917 found positive evidence of infection in all of 50 autopsies on adults and in nearly 24 per cent of a group of 93 children, the latter showing a

far higher figure in the adolescent years. These findings led Opie to remark, "Almost all human beings are spontaneously vaccinated with tuberculosis before they reach adult life."

In 1922, Watson reported positive findings in 82 per cent of his autopsies, and in 1925 Lambert and de Castro Filho reported a rate of 72.8 per cent in a large series from Brazil. As late as 1927, Todd still found evidence of tuberculous infection in 69 per cent of autopsies done in Edinburgh on patients who had died of some cause other than tuberculosis. Such evidence indicates rather clearly that the decline in infection rate has not kept pace with the mortality from this disease.

The present study was carried on at the Washington County Hospital in Hagerstown from September, 1938, to August, 1940, all autopsies being performed by the same pathologist. There were 176 autopsies during this period, which represented 45 per cent of the deaths that occurred. Eleven of these were rejected because they were not complete post mortem examinations, leaving 165, which are included in this report. Cases of active tuberculosis are not admitted to the hospital. The population of Washington County is semirural and most of the patients were long residents, from all classes of society and of the white race (there were only 4 Negro adults in the group).

Thirty-two of the 165 necropsies were done on children, and 133 on adults. For the whole group, positive findings were recorded in 65, or 39.4 per cent, which is just half of Naegeli's findings, 79.9 per cent, when he included all ages.

Considering only the adult group of 133 cases, the positive evidence of infection yielded 47.4 per cent again strikingly near half the number of adults found to be infected by the earlier researches of Naegeli, Burkhardt, Opie and others. In this series, there were 5 cases in which infection was suspected but could not be proved pathologically. If these are included, the percentage stands at approximately 50.

This finding of almost 50 per cent of positive tuberculosis among an unselected group of semirural population indicates that the frequency of tuberculosis is still sufficient to be alarming. If one assumes this experience as typical of the country as a whole, which seems reasonable, one must still face the fact that at least half of all adults have suffered invasions by the tubercle bacillus active enough to leave discoverable scars. This is disconcerting in face of the far greater fall in the death rate from the disease.

At the same time, there is some compensation in the discovery revealed by this study that only half as many people who have suffered tuberculous infection actually die of the disease as died forty years ago. The infection rate has been reduced to 50 per cent, and the mortality to 25 per cent of that in 1900. A number of factors have probably contributed to this gratifying preponderance in the decline of the death rate. Better sanatorium care and the management of cases have undoubtedly made a large contribution. The fact that lessening of the infection rate has apparently shown acceleration in the past fifteen or twenty years brings comfort to those engaged in both the preventive and the therapeutic aspects of tuberculosis control. A 50 per cent reduction in the reservoir of spreaders must certainly mean that fewer contact cases are today submitted to massive and repeated doses of infected material. The contribution of compression therapy and surgery to this result can but be inferred. Those who advocate freer use of these measures certainly would

seem to have little for which to apologize in the evidence presented by this study.

However, other factors in the picture, perhaps, deserve first mention. Isolation is the time-honored scheme for the control of epidemic, infectious disease. It is a significant coincidence that during the period when tuberculosis mortality was reduced to one quarter its 1900 level and the infection rate cut by 50 per cent, the sanatorium beds in this country increased from about 6000 to 100,000. It would be idle not to recognize this prophylactic procedure as an outstanding influence in lessening opportunity for infection among the general public.

The result of this procedure would have been far more striking had it been possible to arouse the medical profession to its responsibility in finding the early case and effecting its immediate isolation. Unfortunately, this is one of the weaker links in the control program. From three quarters to four fifths of all patients admitted to sanatoriums are still found to be in the advanced stages of the disease, already probable spreaders of the infection to others. More professional education, both undergraduate and postgraduate, is still needed to impress on physicians how truly further progress in tuberculosis control rests in their hands.

Popular health education and school hygiene have also played their parts in reducing opportunities for infection. Beginning with teaching the infectivity of sputum, the transference of disease through common utensils, uncleanness in restaurants and the menace of infected food handlers, instruction has proceeded to the point where even an open case is of relatively little danger to the patient's fellows if both he and they exercise the prophylactic measures now recognized as largely effective.

Finally, better housing, elimination of industrial hazards, more applied knowledge of the laws of nutrition and a growing consciousness of the significance of personal and community hygiene have played their part in reducing the transmission of tuberculous infection from case to contacts.

A highly significant factor in this study is the observation that reduction of infection as shown at autopsy has been at least as rapid among infants and children as among adults. These younger members of society can make no personal contribution to their own protection. They must rely on that of others—nurses, teachers, parents and relatives. Cutting their infection rate in two, as well as that of their elders, is clear proof that a better-informed public is making an increasingly effective fight against spread of this disease.

Frost, in discussing the eradication of tuberculosis, wrote as follows:

Tuberculosis also differs from the other directly transmitted respiratory tract infections in that its mortality has declined consistently for the last fifty years or more and continues to decline in every part of this country for which adequate statistics are available. It is not directly established by comparable statistical evidence that there has been a proportionate decrease in the prevalence of infective cases of the disease, taking into consideration not only the number of cases but duration of the open stage. However, there appears to be no good reason to doubt that the prevalence of open lesions effective in spreading the tubercle bacillus has diminished progressively, and continues to diminish in each considerable period of time.

However, it must not be overlooked that, according to present autopsy records, the reservoir of adults infected with tuberculosis at one time or another in their lives

still amounts to half the population. Therefore, tuberculosis can still flare up again whenever external conditions turn to the worse for the bulk of the people. Without such a reverse, there exists the hope that further effort in the campaign against tuberculosis will some day lead to a complete eradication of the white plague.—Reprinted from *Tuberculosis Abstracts*, November, 1941.

## NOTES

Twenty-three appointments to the teaching and research staff at the Harvard Medical School, effective during the present academic year, were recently announced as follows: assistants in medicine, Theodore B. Bayles, of Jamaica Plain, M.D. Harvard '36, L. Tillman McDaniel of Denison, Texas, M.D. Harvard '36, and Thomas A. Warthin, of Boston, M.D. Harvard '34; research fellow in medicine, Charles C. Bailey, of Boston, M.D. University of Virginia '37, Ephraim P. Engleman, of Cambridge, M.D. Columbia '37, Cutting B. Favour, of Washington D. C., M.D. Johns Hopkins '40, Abraham S. Freedberg of Newton, M.D. Rush Medical College '34, Harry I. Klinefelter, Jr., of Baltimore, M.D. Johns Hopkins '31, Julian E. Levi, of Boston, M.D. Johns Hopkins '38, Philip S. Owen, of Chester, Connecticut, M.D. Yale '37, and James V. Warren, of Columbus, Ohio, M.D. Harvard '35; research fellows in surgery, Rutledge W. Howard, of Jersey City, New Jersey, M.D. '37, and John E. Adam of Brookline, M.D. Harvard '39; research fellows in physiology, Douglas D. Bond, of Cambridge, M.D. University of Pennsylvania '38, Robert Galambos, of Cambridge, Ph.D. Harvard '41, and Manoel da Fronta-Moreira, of Rio de Janeiro, Brazil, M.D. National School of Medicine, Brazil, '40; assistants in ophthalmology, Franklin I. Burger, of Wellesley Hills, M.D. University of Michigan '36, and Thomas J. Cavanaugh, of West Roxbury, M.D.C.M. McGill '35; research fellows in pharmacology, Enrique M. de Espanes, of Cordoba, Argentina, M.D. University of Cordoba, Argentina, '28; teaching fellow in anatomy, Gabriel W. Lasker, of Brookline, A.M. Harvard '40; assistant in pediatrics, Winthrop I. Franke, of Jamaica Plain, M.D. Harvard '38; research fellow in biological chemistry, Thomas R. McLin, of Peoria, Illinois, M.D. Western Reserve '39; research fellow in legal medicine, Herbert S. Breyfogle, of Brookline, M.D. University of Chicago '37. In addition, Norman Weissman, of Boston, Ph.D. Columbia '44, was appointed a research fellow in dental medicine.

Dr. Frederic A. Gibbs, of Boston, was recently given one of the two annual Mead Johnson Awards by the American Academy of Pediatrics for his contributions to present-day knowledge of epilepsy.

Twenty-one Charles Hayden Memorial Scholarships were recently awarded to members of the first-year class at Tufts College Medical School. These scholarships are made possible through a gift of \$20,000 by the Charles Hayden Foundation, and they are awarded on the basis of financial need to young men who intend to enter the general practice of medicine. The recipients were as follows: Ward A. Albrow, Winchester; Frank A. Avola, Boston; George R. Bancroft, Jr., Winchester; Louis Burk, Chelsea; Joseph L. Cafarella, Malden; Robert C. Cornell, Mountain Lakes, New Jersey; Brendan F. Crotty, Jamaica Plain; Albert A. Delery, Somerville; Gordon N. French, Newton Center; Leon Herman, Brighton; Francis I. McCarthy, Chelsea; David E. McGaw, Winthrop; George B. McManama, Waltham; Stanley J. Mikalonis, South Boston; Edward S. Murphy, Jr., Belmont; Morris Sup

witz, Chelsea, John DeV Sweeney, Waltham, George J Tsolas, Watertown, George L Tully, Jr., West Newton, Lansing P Wagner, Cambridge, and William J White, Jamaica Plain

## CORRESPONDENCE

### INTERN SUPPLY AND DEMAND\*

*To the Editor* The editorial in the October 2 issue of the *Journal* concerning 'Intern Supply and Demand' contains assumptions both expressed and implied which we believe warrant discussion.

It is stated, 'Even if medical schools could increase their output and thus satisfy the demands for intern service . . . this merely means that a serious oversupply of practicing physicians would eventually occur, since the very increases in the utilization of hospitals that brought about the present disproportions have already diminished the practice of domiciliary medicine.' Though we may be mistaken, it appears that this statement points out that the field of private practice is growing smaller and, therefore, that the graduate output should be at a relatively fixed number, which in fact has been maintained for the past ten years. Yet it also recognizes that hospitals have been meeting a larger and larger medical need, both absolutely and relatively, in the community. It is evident, and the editorial expressly agrees, that the policy of a fixed supply of medical graduates must mean, in general, inadequate medical care where at present the greatest need exists. What should be done about this problem? To discuss it by deploring unfair competition among hospitals for interns and by warning the unwary intern against financial lures of inferior hospitals hardly seems adequate.

Whose needs should decide, in all fairness, the yearly number of medical graduates: the demands of organized medicine for a safeguarded private practice or the actual changing medical needs of the entire community? The editorial appears to imply that the yearly supply of medical graduates must be determined by the opportunities for the private practice of medicine. Yet one must agree that this criterion is hardly satisfactory if it prevents adequate care of the sick. In fact, an attempt to safeguard private practice at the expense of adequate care may well result in a dissatisfaction that will shorten the road to governmental medicine.

We should squarely face the problem of the community's need, which is, more physicians in hospitals. Is it not conceivable that if the number of physicians in hospitals bore a more reasonable relation to the increasing demands of the community on the hospitals, the present number of physicians would be more nearly adequate to the demand made on medicine? The problem, therefore, is not how to limit the number of medical students, but how to induce physicians to stay in the hospitals beyond the ordinary internship period.

The answer must be looked for in the reasons why interns leave the hospital. The intern's life as a rule consists of overwork, poor food and dependence or poverty. The present shortage of interns means increasing routine laboratory work and therefore steadily deteriorating educational opportunity in the internship. For a proper medical education, a longer period of hospital work is now necessary. This prolongs the individual's dependence. The long training period is extremely expensive, and as Dr Alan Gregg, of the Rockefeller Foundation, has recently pointed out, this means that medical graduates are being drawn from an increasingly restricted

financial group of society. This is hardly an intelligent or a democratic procedure, and Dr Gregg has suggested the subsidization of medical training as a remedy. Furthermore, recent advances in medicine have shown that, in every field, a man must have the fundamental satisfactions of life. This is the more true for physicians, who have to deal with tremendous numbers of patients who have failed in attaining some of these satisfactions. The blind cannot lead the blind! It follows that the medical graduate is in urgent basic need of a home, wife, children and financial independence. Is it any wonder, then, that medical men now yield unquestionably to the financial and other rewards of private practice?

It is obvious, therefore, that to induce physicians to stay in the hospitals, where they have to be to meet the needs of the community, the present setup will have to be altered fundamentally to permit them to lead normal lives as soon after graduation as possible. The Oslerian tradition of monasticism in medicine is incompatible with the demands of the modern physician. Nor does the easy statement of the older clinician, 'It wasn't like that when I was an intern,' get us very far, he has forgotten that he used to travel by horse and buggy, which he was delighted to see disappear.

We have spoken with many interns and resident physicians about the matters discussed in this letter. They agree that the points raised are well worth discussion from the point of view of the medical needs of the community, of enlightened medical practice, of the intern and of the practitioner.

### A GROUP OF RESIDENT PHYSICIANS

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In the editorial space was necessarily limited, and the *Journal* is very glad to print further discussion. The names of the six residents who signed the letter have been omitted, at their request.

In considering the problem, one should bear the three following thoughts in mind: the fixed number of medical graduates represents the greatest possible output of American medical schools unless their present facilities are enlarged or their present educational standards are lowered, or both—whether it is the optimum number and why are other matters it is also a fact that the community must absorb and support the yearly supply of medical graduates—whether it does so through the channels of hospital, domiciliary, public or private care is a secondary matter, and will eventually be determined by the laws of supply and demand and the disproportions that are now apparent between the supply of and the demand for interns need correction, which was the reason that the subject was brought up for discussion.

The most immediate corrective measure would appear to be a lengthening of the years devoted to hospital practice, thus shortening those subsequently devoted to extramural activities, with whatever financial or other adjustments are available or obtainable therefor. Other, and perhaps more effective, corrections are no doubt possible. These must naturally be made in the interest of the recipients of medical care rather than in that of any group of its dispensers. Ep

### Erratum

In a letter by Dr George Saslow published in the November 6 issue of the *Journal*, the word 'no' was inadvertently omitted from the first sentence in the second paragraph. The sentence should read as follows: 'It might be thought that no special attention need be given

these points in the northern part of the United States, but this is apparently not so."

## BOOK REVIEWS

*Textbook of Pediatrics.* By J. P. Crozer Griffith, M.D., Ph.D.; and A. Graeme Mitchell, M.D. Third edition, revised and reset. 8°, cloth, 991 pp., with 220 illustrations and 66 tables. Philadelphia: W. B. Saunders Company, 1941. \$10.00.

In this, as in previous editions, the wide range of pediatric interest is covered with remarkable thoroughness when one considers the limitation of space imposed by a single volume. The new edition has been entirely rewritten, and the first portion, which deals with growth and development, has been materially enlarged. This is the field in pediatrics that the general practitioner who graduated several years ago will find particularly useful.

It is difficult not to deal in superlatives in considering this book, which can be unqualifiedly recommended both to students and to practitioners of medicine.

It is a tragic circumstance that since the book was written both the authors have died—Dr. Griffith on July 21 and Dr. Mitchell on June 1, 1941. This third and final edition by these two eminent pediatricians is therefore especially significant.

*Hutchison's Food and the Principles of Dietetics.* Revised by V. H. Mottram, M.A. (Cant.), and George Graham, M.D. (Cant.), F.R.C.P. (Lond.). Ninth edition. 8°, cloth, 648 pp., with 30 illustrations. Baltimore: Williams and Wilkins Company, 1940. \$6.75.

The ninth edition of this well-known\* book is a welcome addition to medical literature. The original volume was first published in 1900, so that in forty years not only have nine editions been issued, but each edition has been many times reprinted. It has become a standard book on the subject, in both Great Britain and this country, and is a lasting monument to Sir Robert Hutchison, who originally compiled the material and gave the medical profession one of the outstanding books on the scientific aspects of nutrition and the treatment of diseases.

There have been changes in the knowledge of nutrition, particularly in relation to vitamins, since the eighth edition was published. In addition, the world has become conscious of the value of foods, not only in the treatment of disease, but in the general welfare of populations, particularly in relation to war conditions. Wartime has always proved an incentive to the study of dietetics, and the present era is no exception to this rule. The new edition of this book considers the more recent advances in the nutritional field.

*Hemorrhagic Diseases: Photo-electric study of blood coagulability.* By Kaare K. Nygaard, M.D. 8°, cloth, 320 pp., with 59 illustrations. St. Louis: The C. V. Mosby Company, 1941. \$5.50.

This book represents a serious attempt to study the mechanisms of blood clotting by the use of a photo-electric technic. A "coagelgram" is obtained by photo-electric scanning of the clotting of recalcified plasma. To the reviewer, the detailed descriptions of the various steps in the clotting process, as mechanically observed, are of less interest than the excellent reviews of the literature and the discussions of the nature of the coagulation problem. It cannot be denied, however, that the introduction of exact standardized methods in any problem is desirable. In the discussion of thrombocytopenic purpura,

perhaps too much attention is devoted to the minor changes in plasma clotting time and to the highly hypothetical "thrombocytolytic activity of the entire reticulo-endothelial system." A good discussion of hypofibrinogenemia, both in adults and in the newborn, is presented.

Whether or not any unusual light has been shed on the problems of coagulation in this monographic presentation of the author's numerous experiments, there can be no question that Nygaard has performed a distinct service by his painstaking and original investigations, which were for the most part performed while he was a fellow in surgery at the Mayo Clinic.

## NOTICES

### GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held at the Beth Israel Hospital on Tuesday, December 2, at 8:15 p.m.

#### PROGRAM

The Practice of Medicine in Historical Perspective. Dr. Henry E. Sigerist, professor of the history of medicine and director of the Institute of the History of Medicine, Johns Hopkins University School of Medicine. Discussion will follow by Drs. Hugh Cabot, Reginald Fitz and James C. McCann.

### BOSTON DISPENSARY

There will be a clinical staff meeting of the Boston Dispensary in the Pratt Hospital Auditorium on Wednesday, December 10, at 12:30 p.m. Dr. Warfield T. Longcope, physician-in-chief, Johns Hopkins Hospital, Baltimore, will speak on "Virus Pneumonia," and the discussion will be led by Dr. Maxwell Finland. Luncheon will be served at 12 m. All interested members of the profession are cordially invited to attend.

### BOSTON HEALTH LEAGUE

A special meeting of the Boston Health League will be held at Perkins Hall, 264 Boylston Street, Boston, on Friday, December 5, at 12:30 p.m. Dr. Harold C. Stuart will speak on "Nutrition in Unoccupied France."

### JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston  
Lecture Hall, 9-10 a.m.

#### MEDICAL CONFERENCE PROGRAM, DECEMBER

Wednesday, December 3—The Pathologic Physiology of Hypertension: Some recent developments. Dr. R. W. Wilkins.  
Friday, December 5—Errors in Cardiovascular Diagnosis. Dr. Paul D. White.  
Monday, December 8—Clinicopathological conference. Dr. Warfield T. Longcope and Dr. H. E. MacMahon.  
Tuesday, December 9—Medical clinic. Dr. Warfield T. Longcope.  
Wednesday, December 10—Atypical pneumonias. Dr. Lowrey Davenport.  
Thursday, December 11—Epidemiology of Hemolytic Streptococcal Infection. Dr. Chester S. Keefer.  
Friday, December 12—Medical clinic. Dr. Warfield T. Longcope.  
Saturday, December 13—Treatment of Pneumococcal Pneumonia with Sulfadiazine and Serum (motion picture).

(Continued on page viii)



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## WHY FIRST AID?\*

A WILLIAM REGGIO, M.D.†

BOSTON

THE medical literature is filled with articles about the treatment of injuries and the shock accompanying them. The public expects the physician to accomplish miracles in saving the life of some smashed up victim or in restoring him to normal again, no matter what the accident or in what condition the patient has been brought to the hospital.

Physicians not infrequently criticize the layman for the way in which such injured persons are brought to them, but, it is pertinent to raise the question, What is the medical profession as a whole doing to improve the first-aid care of the victims of accidents?

The laymen are doing considerably more in that direction than physicians, who as a group, I am afraid, are considerably to blame for this state of affairs. Their greater interest in the treatment of injuries after the victim has been taken to the hospital and their failure to emphasize the care to be given such a person from the very instant after the accident occurs are major factors.

To be sure, more recently, greater attention is being paid to the immediate or first care that these victims require, but most of the emphasis is still being placed on the care that comes after the ambulance has "rushed the victim to the hospital" (with or without police escort).

Although what is done for such patients once they are in the hospital is of the utmost value and deserves much space in the literature, one should not forget that it is to the physician's advantage, as well as to that of the patient, to have these cases brought to the hospital with as little additional shock and damage as possible. Great care should be taken immediately after an accident, and that is when first aid finds its place.

First aid is the immediate and temporary care

given by trained persons in case of accident or sudden illness before the physician takes charge." This definition is taken from a manual‡ recently published by the American Red Cross.

In 1940, there were 8,800,000 accidental injuries in the United States, 93,000 of which resulted in the death of the victim. Of these deaths, 32,600 were due to automobile accidents, and 25,800 to falls. This means that out of 24,000 accidents that occur each day in the United States, 255 of the victims die. As of April, 1941, there were about 186,000 physicians in this country. With 170,000 accidents occurring each week, it would mean that every physician—if all accidents were immediately seen by a physician as the first person to arrive on the scene—would care for 48 accidents a year. Of course, this is quite useless figuring, except so far as it brings out the fact that the great majority of accident victims must receive their first aid care from a layman who "holds the fort" until the services of a physician can be obtained.

The first-aid care given by a layman often makes the difference between life and death for the victim, and it is reasonable to suppose that a physician will be very grateful that the case has been adequately cared for by some layman, who has thus given the physician a fighting chance to get his patient through alive.

The training of laymen in first aid was begun by the American Red Cross in 1910, when the first class was taught and the first certificates for the successful completion of the course were issued. From 1910 to 1935, the first million certificates were issued, from 1935 to 1939, the second million, and from 1939 to 1941, the third million; and now the number of people asking for and receiving instruction in first aid is nearly double that of a year ago. The fourth million certificates are now

\*Read by title at the annual meeting of the New England Surgical Society, Harvard New Hampshire September 5, 1941.

†Instructor in surgery, Harvard Medical School, assistant visiting surgeon, Massachusetts General Hospital, chairman, First Aid, Boston Metropolitan Chapter, American Red Cross.

‡First Aid Manual for Civil Defense Units. 16 pp. Washington: American Red Cross, 1941.

well on their way, 410,966 having been issued during the last twelve months. For the same period, that is, from July 1, 1940, to June 30, 1941, 10,406 instructor's certificates were issued; several thousand additional instructors were trained during this period, but all the certificates have not as yet been issued. Also, as of June 30, there were available for use as active first-aid instructors 30,871 men and women. Most of these are laymen trained and retrained by the Red Cross, but some are physicians appointed by application only.

The American Red Cross offers four courses in first aid. The junior course gives boys and girls from twelve to seventeen years of age instruction in the principles and application of first aid. This course requires a minimum of fifteen hours. Then comes the standard course, which calls for a minimum of twenty hours of teaching and usually requires nearer twenty-five hours for satisfactory completion. The standard course may then be followed by an advanced course, which requires a minimum of ten more hours. Finally, there is the course for instructors in first aid, which requires an additional fifteen hours of teaching after completion of the standard and advanced courses. Both written and practical examinations are given at the end of all these courses and must be successfully passed if a qualifying certificate is to be obtained. Instructors are authorized to conduct the junior, standard and advanced courses, but not the course for instructors, which is given only by specially qualified and authorized instructors approved by headquarters of the American Red Cross in Washington.

There has been and there still is a certain amount of unfavorable criticism and objection on the part of some physicians to the rendering of first aid by laymen. Although poorly administered first aid may be worse than none, proper and adequate first aid, correctly given by a trained layman, may often be the deciding factor between survival and death of the victim of an accident. Of course, there are good first aiders and poor ones, as there are good physicians and poor ones.

Just why this sporadic opposition to the training of laymen in first aid is still maintained by a certain number of physicians is in one way difficult to understand, although in another way the answer is simple. In plain language and without any apologies for making such a statement, the underlying reason for this attitude is ignorance of what first aid really is. They do not know how or what the layman is taught. They criticize the methods taught because these methods do not happen to coincide with what they themselves would do. They have not taken the trouble

to find out anything about first aid and not infrequently assume this superior attitude to cover up their own ignorance.

A well-trained first aider can teach a doctor many a valuable trick, provided the doctor is not too superior to be willing to learn from a layman. How many doctors out of the 186,000 in this country are familiar with what is taught in a course in first aid, or are really qualified, off-hand, to teach such a course to laymen? It is doubtful if 4 per cent, or about 7500, could do so on the instant, without first learning more about the subject.

Quite a number of physicians who are interested and are willing to be instructors take the standard, advanced or instructor's course to familiarize themselves with the methods they are to teach. It is unfortunate that any doctor of medicine who is a graduate of a Class A medical school, and who is without Red Cross training, may be appointed an instructor in first aid to teach the junior, standard and advanced courses merely on his request for a certificate from the Red Cross. On the other hand, graduates of unapproved medical schools or members of the cults would have first to take the standard, advanced and instructor's courses and pass them successfully, before they could receive a certificate authorizing them to teach.

First aid as rendered by a physician not only may be but frequently is a very sad substitute for what could be done by a trained layman under similar circumstances. Naturally, the layman steps aside when a physician arrives to assume responsibility for the care of a victim, but often the injured person would have received better first aid had the trained layman been allowed to render it instead of the doctor. This is particularly applicable to fractures at the scene of an accident.

Trained laymen know how to use a Keller-Blake leg splint, or a notched board or rake as substitutes, and how to apply fixed traction for safer transportation of the victim. Many physicians do not even know what a Keller-Blake splint is, much less how to apply one, and even less how to improvise or use substitutes.

Another difficulty too frequently occurs during a course in first aid. The class or the instructor invites a physician to attend an exercise and give advice or answer questions. The result is that the physician often condemns traction splinting or some other method of rendering first aid because he, himself, is opposed to such a procedure (or ignorant concerning it), or is personally convinced that a trained layman is not qualified to employ such a method. Of course, it is discourag-

ing to the class and the instructor (who are doing their utmost to be efficient) to be casually informed, with the voice of pseudoauthority, that they are all wrong because that particular physician happens to disagree with or be ignorant concerning methods approved by the American Red Cross, the American College of Surgeons, the Bureau of Mines, the American Association of Railroad Surgeons, the National Safety Council, the National Ski Patrol and numerous similar organizations, to say nothing of physicians outstanding in the field of traumatic surgery throughout the country. The underlying cause of this trouble lies in the fact that medical schools do not teach first aid to their students, and that their graduates consequently know nothing about the subject. It is not the fault of the students but of their instructors.

In a checkup of the medical schools of the country conducted during 1940 by a special committee of the American College of Surgeons, it was found that not a dozen medical schools taught anything about first aid, except for the application of emergency splinting as part of fracture instruction. In half these schools, attending a course in first aid is optional for the students. First aid should be a required course in the first or second year in every medical school.

I take the liberty of quoting two sentences from a personal communication on this matter, since they so aptly bring out the point in question.

First, it serves to give some practical medical work and useful information to the students in their first and second years that they are able to assimilate at least as well as Boy Scouts and those who attend Mothers Meetings. In the second place, since many of these boys take positions as camp counselors or camp physicians in their summer vacations, a first aid course is of more value to them under these circumstances than the other courses of their first two years are biochemistry, pathology, bacteriology and the *Lives of the Saints* are all of about equal value for a camp counselor and camp physician.

Most medical students and even the younger hospital interns could be put to shame in the rendering of first aid by almost any First Class Boy or Girl Scout or trained layman.

Physicians should consider honestly whether they are able — offhand — to teach a layman the following procedures of first aid care according to the standards of the American Red Cross: the prone pressure method of artificial respiration; detection of the signs and symptoms and first aid care of snake bite, the application of a Keller-Blake and a Murray-Jones splint; traction splinting with some substitute when these splints are not avail-

able; bandaging a hand, ankle or foot with the triangular bandage, open or folded.

It is no simple matter to render adequate first aid on the open road when materials have to be improvised and the complete equipment of a hospital accident room is many miles away. I have seen injured people brought to the hospital who had received first-aid care from a physician, and it has struck me that I should much prefer to have been handled by a well trained layman under similar circumstances.

This training of laymen should be encouraged, and the physician is the one who can give this encouragement, because in his contact with his patients and with community interests he can, if he will take the trouble to inform himself beforehand concerning it, arouse interest.

All police and fire departments should have their men trained in first aid. This is being slowly accomplished against considerable opposition. One must realize that people taking the course do so voluntarily and usually during their free time, and that there is no financial reward connected with it. It is just one of those unselfish things that may bear fruit if the emergency arises.

The fact has frequently been commented on that when a person knows how to render first aid, it makes him more careful to avoid accidents because, knowing the result of an accident, he is likelier to think twice before running such a risk.

When motoring along the highways, one sees quite a number of signs — usually near gasoline stations — indicating the location of a highway emergency first-aid station under the auspices of the American Red Cross. This means that the men connected with that station have taken the standard course and are qualified and equipped to render first aid when necessary. Many large industrial concerns, gas, electric and telephone companies, department stores — in fact, almost any manufacturing or public service organization in the country — have a department that concerns itself with the training of employees in first aid. The first step is usually to have a certain number of employees take and pass the standard, advanced and instructor's courses, and then, in turn, give the standard course to other employees.

Another thing that, by the thoughtful co-operation of the press, could be changed is the spectacular reporting of "rushing" injured people to hospitals. The newspapers seem to love the dramatic appeal of this word and fail to realize that, by this excess of speed, not only are other people and vehicles endangered, but the unfortunate victim has shock increased by the joggling

and tossing about that he gets during his ride. If the ride were less hasty and at a moderate, safe speed,—and, if possible, in an ambulance,—the victim would, not infrequently, arrive at the hospital in better shape than when he started. However, the public loves the dramatic whether it costs a life or not.

In the present national emergency, defense councils or committees on public safety have been set up in all the states of the Union. One of their activities deals with the care of the injured as a result of property damage of one sort or another. In connection with this, each community is providing a large number of air-raid wardens, who are to be trained in their particular tasks of coping with property damage and attempting to give the bare essentials of first aid to injured people as well.

In Massachusetts, as a result of the insistent demand of the State Committee on Public Safety,

the American Red Cross has added a short course in first aid taught only to persons enrolled as air-raid wardens; this short course in no way supplants the standard course. In fact, all persons taking these ten hours of instruction are urged to follow it up, if possible within six months, with the standard course. The distribution of *First Aid Manual for Civil Defense Units*, printed by the American Red Cross, is confined in Massachusetts to officially recognized defense groups.

Physicians have a firm conviction that "life is more valuable than property," and strive in every way to preserve that life. In the event of an accident, the care or treatment begins at once or as soon as possible after the occurrence. With some 9,000,000 accidents taking place each year, it seems reasonable that physicians should act according to what they say about the value of life—in other words, acknowledge that first aid is worth while. Why first aid? Why NOT?

374 Marlboro Street

## THE CARDIOVASCULAR ASPECTS OF AVIATION MEDICINE\*

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THE introduction of aircraft into warfare during World War I gave promise that if another cataclysm should eventuate it would have an even more extended application. The present conflict has fulfilled that promise to a greater extent than anyone had anticipated. The prediction that success in war would be largely dependent on aerial supremacy is being vindicated daily. The position of aircraft in the world today is exemplified in the extended interest in aviation medicine displayed by the medical profession. This interest springs not only from curiosity but from a patriotic desire to render to the nation the wholehearted and complete service that is expected of American physicians. It is in times of stress like the present that we of the regular services have to depend on that assistance, and our humble appreciation can be understood.

The problem of the flight surgeon is included in the selection of flying personnel and keeping them in the air.

Aviation medicine is peculiarly subclinical in its field of interest and application. In this respect, it is the acme of preventive medicine. We are most exacting in the choice of our clientele, and

the art of our practice is designed to preserve a degree of fitness for a peculiarly exacting mode of life, which is different from and of higher degree than that necessary for any other field of endeavor. For these reasons, it is tremendously necessary for us to have available and make use of any and all armamentaria that will make our selections sound and our practice healthy.

The selection of flying personnel requires, first of all, freedom from organic disease. This is true of the entire economy but particularly so of the cardiovascular system because of the unusual strain to which it is subjected in flying. The heart is insulted by flying. In recent years, we have become more and more impressed with the importance in the development of cardiac disease of what may be called the pace of life. We may differ in our opinions of the relative significance of this factor in the development of, specifically, coronary thrombosis, as compared to infectious disease, heredity, diathesis or other causes, but the fact remains that the incidence of demonstrated coronary disease has risen *pari passu* with an increase in the tempo of existence in the present highly mechanized and speedy era. Flying is outstandingly of this order. It depends on speed and its concurrent, rapid change of environmental aspect and on the necessity of swift and accurate

\*The Henry Jackson Lecture, delivered before the New England Heart Association, May 2, 1941.

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adjustment to these changes. Whether or not this degree of stress is controlling in the development of organic cardiac disease, it would be folly to permit a person deliberately to subject himself to it if he already has evidence of actual or potential organic disease.

Flying requires adjustment to a new and unusual set of circumstances in its three-dimensional fields. With rapid changes in altitude come the problems of anoxia and high accelerations. The burden on the heart of maintaining adequate circulation in the presence of high degrees of anoxemia is well known. The profound changes in blood distribution incident to the centrifugal forces encountered in certain maneuvers place a peculiar burden on the circulation, in which the heart has its share. The responsibility of repeatedly and suddenly requiring an effort to preserve the circulation against profound reduction and inadequate filling of the right heart is peculiar to flying. These are unhuman circumstances, and for that reason especially trying. They are not reasonable tasks to present to a heart unless it is free from actual or incipient organic inefficiency.

For the determination of actual or incipient organic heart disease, we must depend on the diagnostic methods commonly used in physical examination. Careful history, keen inspection, accurate percussion and clear auscultation continue to be the most reliable diagnostic tools. Adjunctive aids in the form of electrocardiograms and x-ray plates must remain supplementary for those cases in which commoner methods of examination do not suffice to make the diagnosis clear. Under present circumstances, when it is necessary to examine and certify large numbers of flying applicants, it is administratively impractical to include in the records the comprehensive and complete data desirable in a clinical case history or for the preparation of a scientific treatise.

This does not mean that these diagnostic aids should be neglected. The electrocardiograph should have a well-established position in aviation medicine. It would be tremendously desirable to have on record a tracing of every aviator when he begins training. For purely diagnostic purposes and for the detection of arrhythmias, blocks and coronary disturbances, such data would be invaluable. For interpretation in terms of subsequent tracings, taken incident to routine periodic examination or when indicated by intercurrent findings, their value is manifest. It is generally agreed that these original tracings should be made and filed.

Again, taking routine periodic tracings, particularly in certain age groups, would be highly

desirable. For a complete record on which to be absolutely sure that the heart continues in high efficiency, such routine examination must be considered indispensable. But the desirability of this procedure must be weighed in the light of administrative capabilities.

To equip all points of original examination with apparatus would seriously tax the industry and would represent an outlay of federal funds that might be justly criticized in time of pressing need for rigid economy. To staff all recruiting stations with trained personnel to make the tracings would require either that civilian institutions be stripped or that intensive training be instituted. To assign to suitable stations enough physicians capable of accurately reading the tracings in the tempo required for defense would deplete the ranks of cardiologists needed by hospitals and educational institutions. How accurate electrocardiographic readings can be obtained on all incoming aviators with sufficient expedition to eliminate those showing sufficient evidence to debar them from flying, not to prevent those whose tracings are well within normal limits to begin training and not to impede a pressing training schedule is a serious question.

At the moment, the problem of fitting electrocardiography into selection of prospective aviators is more urgent than the routine examination of certain age groups. In time of peace, when schedules can be sufficiently flexible to arrange for the transfer of all pilots in certain age groups to central points for electrocardiographic study, the best that could reasonably be expected would be annual examination of pilots over forty years of age. In times of emergency, such as the present, routine stated examinations are virtually impossible. In answer to the argument that one pilot grounded would pay for the procedure, it can be pointed out that separation of a considerable group from points of strategic importance might jeopardize a campaign. The solution to this problem is not apparent. It appears certain that a well-organized and competent program, to effect this desideratum, may have to give way to expediency.

In the choice of selection methods on the personality or psychologic side, we are considerably handicapped by the absence of a good working definition of an efficient pilot. One difficulty in validating tests is the fact that we do not have a negative criterion group. This may be said about all phases of the examination. We do not know, for example, whether epileptoid trends make a poor pilot. It may be pertinent to ask the same question about cardiovascular findings. What degrees of variation from the normal mean electro-

cardiogram may be considered perfectly compatible with flying? Again, should electrocardiographic findings that are regarded as definitely contraindicating certain walks of life requiring strenuous exertion necessarily be considered a cause for rejection for flying?

In discussing the cardiovascular aspects of flying in its application to the maintenance of flying fitness, emphasis will be placed on two major considerations: the cardiovascular demands peculiar to flying, and tests for determining cardiovascular efficiency.

In considering the demands of flying at high altitudes, it is safe to conclude that the burden on the heart and blood vessels is no greater than that introduced by the necessity of compensating for anoxemia or oxygen debt incident to other causes. Some forms of athletic exertion are vastly more demanding than the anoxia of high-altitude flying. Indeed, flying is characterized by an absence of physical exertion commensurate with the situation. This has a specific significance in its biochemical aspects. Emotional stress or a misguided urge to get the most out of oxygen equipment may stimulate hyperventilation out of proportion to that required by the amount of carbon dioxide produced by comparative muscular inactivity. The resulting acarbica may have very serious consequences. But this is essentially a chemical problem and is not appropriate to this discussion. From the point of view of anoxia in high-altitude flying, per se, the cardiovascular demands are not excessive.

A chain of physiologic events incident to rapid changes in the direction of flight may be of interest. These alterations result from the introduction of centrifugal acceleration along the long axis of the pilot's body during certain aerial maneuvers. The attendant symptoms—commonly grouped under the term "blacking-out," and popularly ascribed to the pull-out following a dive at high speed—have been extensively described. The physiologic changes have not been so well described.

The physical force involved is the hydrostatic tendency of the blood to be thrown into the lower parts of the body at the expense of the upper parts. In virtually all aerial maneuvers, the direction of gravitational force is normal in that it applies along the vertical axis of the airplane, which means the long axis of the pilot's body. High accelerations along this axis develop most commonly in the pull-out from a dive and in turns of short radius, such as those seen in aerial combat. In the former, these forces may attain the magnitude of nine or ten times normal grav-

ity (9 or 10 g in gravity units). In the latter, they seldom exceed 5 or 6 g, but are usually of longer duration. Both the magnitude of the centrifugal force and the duration of its application are of critical significance. Thus, the greater strength during a pull-out may be of less consequence than the longer duration during a dogfight. For this reason, it is a mistake to consider the effect only in terms of its magnitude. Indeed, the necessity of guarding against the effects in short radius turns is greater than that in pull-outs following terminal velocity dives. This will be even more apparent when the lesser, subclinical symptoms resulting from the physiologic changes are considered.

In considering the changes in blood distribution, it is well to separate the synchronous changes in the arterial and venous columns. If one regards the arterial column from the cranium to the pelvis as fluid confined in a semielastic tube under a pressure of a couple of pounds per square inch subjected to a centrifugal force downward, it can easily be seen that there will result a tendency toward greater pressure and volume in the lower portion at the expense of the upper. The carotid pressure will drop. The venous column is under much less pressure, and the vessels are less elastic. The changes in the venous column are the same as those in the arterial, with this additional feature: if the gravitational force lasts long enough, the column of venous blood is driven below the level of the right heart. Inadequate filling and reduced output result. The carotid pressure drops, because of the force acting on the arterial column; a secondary and more profound drop, incident to reduced cardiac output, follows. For this reason, the venous changes are of greater importance and constitute a direction of approach in attempting a solution.

Given a profound drop in carotid pressure and a greatly increased jugular suction, one is faced with the question of what happens in the closed cranium. If the cerebrospinal fluid in the spinal column were available, one could expect that the sinuses would collapse with the increased arachnoid filling of cerebrospinal fluid. But the cerebrospinal fluid has the same tendency to leave the cranium because of subjection to the same centrifugal force. If arterial blood were available, one might expect a relative increase in the volume of blood in the arteries to compensate for venous collapse. When one remembers, however, that these changes extend over only a few seconds, it is safe to conclude that there can result no compensatory adjustment in relative volumes of the three fluids within the cranium. This leaves only

one vascular end result—a profound reduction of velocity of flow through the cranium. The symptomatology is easily explicable on the basis of the resultant local, transient cerebral anoxia. This explanation is more tenable than the theory of concussion, of sliding of the cerebrum over the tentorium, with impingement of the posterior cerebral arteries and ischemia of the occipital lobes, or of molecular changes in the neurones or any other theory advanced to explain the symptoms of high acceleration.

There is another feature of the symptomatology that supports the concept of cerebral anoxia and points to its most serious import. The experience of blacking out in pulling out from a steep dive is strikingly poignant. There can be no doubt that the pilot has been subjected to a force of tangible magnitude. It will immediately cause something in response—often something wrong. But the anoxia has all the attributes of that produced by any other method. It is identical to anoxia at high altitudes, with the sole exception that it is shorter lived. The most dangerous aspect is its insidiousness in degrees below those resulting in subjective symptoms. As a result of being subjected to high acceleration, a pilot may be the victim of decreased mental efficiency well below the threshold of awareness, but particularly dangerous because of this insidiousness.

The desirability of developing means for obviating the effects of high acceleration is manifest. It is regretted that time, inconclusive proof and, possibly, national advantage do not permit extended discussion of these means. Certain procedures have already proved to be partially effective, and there are scientific findings that lead to other possibilities. The answers will of course be found.

The cardiovascular problem of maintaining flying fitness is largely that of avoiding the development of what has been variously named but fairly uniformly defined as "neurocirculatory asthenia," "effort syndrome," "soldier's heart" and so forth. I prefer the term "staleness" because it avoids the implication that the condition is exclusively a circulatory disturbance, particularly in its etiology. The psychogenic aspects of its etiology are so strong that the early manifestations may be only changes in emotional and temperamental reaction, which often antecede circulatory changes by an appreciable and important interval.

The condition can be accurately diagnosed in the hospital, but when it has progressed to a degree that makes this possible, it is altogether too late for the flight surgeon. If the condition is to be avoided or relieved before it reaches the stage

of hospitalization, it must be disclosed in its earliest and most incipient stages. These patients practically never return to operational flying from hospitals. The task of discovering early evidences and instituting curative measures constitutes the major mission in the practice of aviation medicine.

The competent and experienced flight surgeon, in his capacity of "Dutch uncle" and father confessor,—who lives in daily and nightly contact with his pilots, becomes their confidant and mentor, and is alert to small but significant changes without ostentation,—exemplifies that side of medicine which must always constitute the immediate contact between physician and patient. The principal tools in his armamentarium are his observation, appreciation and compassion. Would that there were more of him today!

During a generation, we have become accustomed to a circulatory efficiency rating using the Schneider index. Six factors—reclining pulse rate, standing pulse rate, increase in pulse rate from reclining to standing, increase in pulse rate following standard exercise, time of return to standing rate, and change in the systolic blood pressure from reclining to standing—are scored on the basis that each is capable of a score of 3. The six are added, giving a total score or index.

The Schneider index has come in for considerable criticism of late, some of it fairly acrimonious. It is claimed that this test does not measure circulatory efficiency. It disregards diastolic and pulse pressures. It gives no indication of circulation time or output per beat. It makes no mention of respiratory indications of circulatory efficiency, such as vital capacity, breath holding and expiratory force. In other words, it is claimed to fall far short of determining what it is supposed to determine.

Before complete condemnation is heaped on the test, however, it may be worth while to consider the use made of it and some of its advantages. In the practice of aviation medicine, the index is applied both in the selection of students and in routine maintenance.

The circulatory efficiency rating is given careful consideration in the original examination. It is seldom, if ever, considered a cause for rejection, per se. If the rating continues low after all possibilities of organic or functional cardiovascular disease have been eliminated and after adequate food and rest have been provided, it must be regarded as an indication of inadequate or unsatisfactory emotional control. If organic disease is disclosed the disease is considered the cause for rejection. If emotional instability remains as the cause for a low rating and is confirmed by other

findings, the instability is the cause for rejection, and the test falls more properly into the neuropsychiatric examination. A low rating is of considerable value in the original examination.

In routine practice, the Schneider index is commonly taken. It is often performed and scored by trained, enlisted technicians. In these situations, it is considered purely as an index, a cue to further study. If it is low because of rapid pulse, fever or intercurrent infectious illness, the index directs attention to the illness. On the other hand, it may be low because of incipient fatigue or neurocirculatory asthenia. In any event, it is used only as an indication for further study. It is particularly significant in the light of a person's normal average as established during a long period of fitness.

The Schneider index may have many shortcomings as a test of neurocirculatory efficiency. We do not use it as such. It has many advantages. It can be administered by comparatively untrained assistants. Anyone who can count and read a watch and a blood-pressure dial can run the test. It requires a minimum of equipment, and can be completed in ten minutes. It is adaptable to service use, wherever that may take it. It gives very valuable information if properly interpreted.

Finally, it has become a tradition. It pervades the literature and drama of aviation medicine. It is of extreme interest to the pilots themselves. It is one thing to explain to a pilot that his cardiac efficiency has improved, as indicated by increased output per beat, or that his vasomotor control is waxing or waning. It is an entirely different matter to tell him that his index is 10, as compared

with his normal index of 14. To personnel trained in accurate mensuration and accustomed to judging on the basis of mathematical readings, a numerical score is tangible and comprehensible. The pilots are sometimes the severest critics of the index. It is completely invalidated when it proves to be high after a bad night. An explanation of the significance of relaxation and composure, coupled with the unstinted confidence of such discussion, serves to cement association, and the index, again, has served a very useful purpose.

Scientific research and study may furnish a much better criterion of circulatory efficiency, but unless it can compete in service adaptability, practicability and comprehensibility, it will encounter opposition in its acceptance.

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The motto of military aviation is, "Keep 'em flying." The service aviators of this country are a choice group of men. They are strong in character, mind and body. They are keen, clear thinkers. They are intelligently critical. They hold a key position in the defense of the nation. They must not be impeded. In all that we do in our mission of keeping them fit to hold that position, we must be scientific, but we must also be practical. Above all, we must not lose sight of the fact that our responsibility is less toward the aggrandizement of general or personal scientific concepts than to the care of the finest group of men in the world. In these days of turmoil and rapidly changing opinion, we must preserve a middle-of-the-road course as mapped by sound, proved facts.



## SUPPURATIVE PERICARDITIS\*

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THE difficulty of diagnosis of suppurative pericarditis and the general agreement among thoracic surgeons about principles of therapy, although not about details, suggest the desirability of periodic restatement of accumulated knowledge of the disease. Although this report is based on consecutive experience with suppurative pericarditis at the Massachusetts General Hospital during the last ten years, and although the total experience is essential background, the advances of recent years require a reevaluation of concepts in relation to the disease and a revision of the therapeutic program in many ways.

The pessimism of the medical profession concerning acute pericarditis was expressed by Cabot<sup>1</sup> in 1926. "We can recognize this disease in only one fifth of the cases and can usually do nothing to cure it. Its clinical importance is therefore small." Winslow and Shipley,<sup>2</sup> in their excellent reviews in 1927 and 1935, however, presented a different picture, at least for purulent pericarditis: about 50 per cent of the cases treated with operation were cured.

A few outstanding facts may be presented at the beginning. The mortality of pericarditis is high because the disease is itself a complication of pre-existing and usually serious infection elsewhere in the body. The diagnosis is difficult and therefore delayed, but the possibility of a favorable outcome is enhanced by early treatment. The only effective therapy is surgical drainage. The recently introduced serologic and chemotherapeutic agents afford additional methods of therapeutic aid that are very promising. A number of articles emphasize the value of surgical treatment of the disease,<sup>4-6</sup> but it appears from the older as well as from the more recent publications that, even with adequate drainage, only half the patients can be saved. Death is often due to multiple lesions elsewhere in the body, as in staphylococcal and streptococcal infections, or to overwhelming infection and exhaustion, as in pneumococcal infection. Bigger<sup>6</sup> reported 9 operative cases, with recovery in 5. Bunch<sup>7</sup> obtained 2 cures in 4 cases. The numerous reports of single successful cases yield little information about the percentage of cures because single failures are seldom

reported. Most of the cases operated on and reported until now were treated before chemotherapy and immunotherapy were generally applied. It seems likely that these forms of treatment may be of great help in the management of purulent pericarditis.

Therapy is discussed in great detail in the following case, for the purpose of emphasizing the advantage of combining all modern therapeutic procedures.

## CASE REPORT

CASE 7 (M. G. H. 753933). A 5-year-old boy was admitted to the Massachusetts General Hospital on February 14, 1940, with a diagnosis of bronchopneumonia and pericarditis. Two months before entry he developed pain in both ears and fever. The middle ear spaces were drained eventually of staphylococcal pus with improvement, but a week later, signs of pneumonia appeared. The pulse was 140, and breathing was rapid and shallow. The ear drums were healed. The cardiac percussion area was greatly enlarged and a pleuropericardial friction rub was heard on the left side. The apex impulse could not be seen or felt and the heart sounds were of low intensity and muffled. There was a paradoxical pulse. The liver edge was palpable, and there was slight edema over the sacrum. The neck veins were distended. Dullness and absence of breath sounds in the left axilla were indicative of pleural fluid. On x-ray examination the heart shadow was enlarged and no pulsations were visualized by kymography. There was a left-sided encapsulated empyema. An electrocardiogram showed tachycardia and elevation of the ST intervals, suggestive of pericarditis.

The pericardial cavity was drained on February 19, without preoperative aspiration. Under local anesthesia, a curved incision was made along the left 7th intercostal cartilage, extending upward to the 5th. The 5th, 6th and 7th cartilages were resected. The pericardium was incised, and 250 cc of purulent fluid, which had displaced the heart to the left, was removed. The lack of smothered heart sounds among the classic signs of pericarditis, was explained by the displacement downward and forward of the heart by the pus, which was encapsulated on the right side above and behind the heart. It had collected in a large cavity in the upper right and posterior portion of the pericardium. The adhesions were broken digitally. The pericardium was sutured to the subcutaneous tissues, and a soft tube was put in place, out of contact with the heart. The tube was connected to a drainage bottle protected by a water seal.

The pus contained a Type I pneumococcus in pure culture. The patient received multiple transfusions and sulfapyridine. Because his blood serum showed no circulating antibodies against pneumococcus by the Francis test, he was given 20,000 units of Type I anapneumococcus serum in sufficient quantities and with such frequency as to maintain a positive test, and the chemotherapy was continued. The empyema cavity was aspirated at intervals. The tamponading procedure of aspirations was elected because the child was too ill to undergo even the simple

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TABLE 1. *Findings and Results of Treatment.*

CASE No	AGE	SEX	PREVIOUS OR COMPLICATING DISEASE	DIAGNOSIS	SIGNIFICANT CLINICAL FINDINGS	OPERATIVE OR AUTOPSY FINDINGS	OUTCOME	MICRO ORGANISM
1 (1929)	45	M	Pneumonia 3 mo before entry with delayed resolution	Made	Enlarged heart muffled sounds and distended veins	500 cc of pus drained at operation no in topsy	Death	Pneumococcus
2 (1933)	60	M	Hernia (operation) and bronchopneumonia	Suspected	Friction rub enlarged heart and distended neck veins	Lobar pneumonia pleurisy, pericarditis (100 cc of exudate) and enlarged liver (2000 gm) at autopsy	Death	Pneumococcus Type 8
3 (1936)	28	M	Lobectomy for bronchiectasis (several mo before entry) and residual empyema	Made	Enlarged heart paradoxical pulse and positive pericardial tap	420 cc and 135 cc of exudate removed by tapping, pericarditis (950 cc of exudate) and enlarged liver (2200 gm) at autopsy	Death	Pneumococcus Type 8
4 (1937)	65	M	Epidermoid carcinoma of left lung and pneumonectomy	Suspected	Signs of cardiac failure without electrocardiographic changes	Pericarditis (150 cc blood tinged fluid) and enlarged liver (metastasis) at autopsy	Death	Pneumococcus Type 1
5 (1937)	2/3	F	Otitis media pneumonia and empyema (drained)	Made	Enlarged heart dysphagia and positive x ray evidence	400 cc pus drained at operation pericardium well drained at autopsy	Death	Pneumococcus
6 (1939)	1/26	M	Pneumonia otitis media and empyema	Suspected	Precordial friction rub	Pericarditis (few cc of exudate), left pleural exudate and lung abscesses at autopsy	Death	Pneumococcus Type 23 <i>Staphylococcus aureus</i>
7 (1940)	5	M	Pneumonia 3 wk before entry empyema	Made	Enlarged heart and liver, muffled sounds paradoxical pulse positive x ray films and electrocardiogram sternal edema and engorged veins	250 cc of pus removed at operation	Recovery	Pneumococcus Type 1
8 (1929)	18	M	Pneumonia 1 wk before entry pleural effusion	Made	Enlarged heart muffled sounds feeble pulse and distended abdomen	Large amount of pus removed at operation	Recovery	<i>Staphylococcus aureus</i>
9 (1930)	10	F	Osteomyelitis of left thigh (drained) and other foci	Made	Friction rub and positive pericardial tap	50 cc of pus removed at operation well drained pericardium and small necrotic abscess in heart muscle at autopsy	Death	<i>Staphylococcus aureus</i>
10 (1931)	5	M	Osteomyelitis of tibia (drained) and meningitis	Suspected	Terminal friction rub	Pericarditis (75 cc of turbid fluid) myocarditis multiple multiple abscesses in liver, spleen kidneys and lungs, and small patch of endocarditis at autopsy	Death	<i>Staphylococcus aureus</i>
11 (1935)	10	F	Osteomyelitis of femur (drained)	Made	Friction rub absent apex beat, distant sounds and paradoxical pulse	Large quantity of pus removed at operation, well drained pericardial sac at autopsy	Death	<i>Staphylococcus albus</i>
12 (1933)	58	M	Cholecystitis and rupture of subphrenic abscess into pericardium	Not made operated on for embolus	None	Large quantity of pericardial pus at operation, communication with subdiaphragmatic abscess at autopsy	Death	<i>Staphylococcus aureus</i>
13 (1938)	22	M	Chronic osteomyelitis with multiple foci	Not made	None	Pericarditis (50 cc of fluid), abscess in heart muscle and amyloidosis at autopsy	Death	<i>Staphylococcus aureus</i>
14 (1939)	3	F	Abscess of thigh (drained), abscess of lung and pneumonia	Not made	None	Pericarditis (100 cc of fluid), 0.5 cm abscess in right ventricular wall and enlarged liver (8 cm below costal margin) at autopsy	Death	<i>Staphylococcus aureus</i>
15 (1939)	40	M	Pneumonia and sepsis	Not made	None	Pericarditis (15 cc of purulent fluid) and abscess in heart muscle at autopsy	Death	<i>Staphylococcus aureus</i>
16 (1939)	38	F	Chronic osteomyelitis (multiple sinuses)	No pericarditis	None	Myocardial abscess (without exudate in pericardium) and amyloidosis at autopsy	Death	<i>Staphylococcus aureus</i>

TABLE I (Concluded)

CASE NO.	AGE	SEX	PREVIOUS OR COMPLICATING DISEASE	DIAGNOSIS	SIGNIFICANT CLINICAL FINDINGS	OPERATIVE OR AUTOPSY FINDINGS	OUTCOME	MICRO-ORGANISM
17 (1932)	19	M	Pneumonia and lung abscess (?)	Suspected	Muffled sounds and enlarged heart	Pericarditis (100 cc of fluid fluid) interstitial edema in muscle, bilateral lung abscesses and enlarged liver (2800 gm) at autopsy	Death	<i>Streptococcus haemolyticus</i>
18 (1934)	48	F	Chronic sepsis otitis media and skin ulcers	Not made	None (tender right costal margin)	Pericarditis (50 cc of purulent fluid) heart muscle not involved thrombosis of liver and pancreas	Death	<i>Streptococcus haemolyticus</i>
19 (1935)	61	M	Pneumonia and empyema	Suspected	Increased muffled sounds	Pericarditis (100 cc of fluid) in pericardial sac thickened to 4 mm extension from pleura and enlarged liver (2150 gm) at autopsy	Death	<i>Streptococcus haemolyticus</i>
20 (1937)	2	F	Pneumonia 2 wk before entry	Made	Enlarged heart muffled sounds paradoxical pulse and positive x-ray evidence	300 to 400 cc of fluid removed at operation with drainage of retropharyngeal abscess and other foci	Recovery	<i>Haemophilus influenzae</i>

maneuver of trochar thoracotomy. Two weeks after pericardiotomy, the residual empyema was drained by rib resection. The patient gradually improved, and was discharged in good condition on April 27. His health has remained excellent since discharge, and he is leading a normal life.

**Comment.** Pericardiotomy in this case may be regarded as a lifesaving procedure, but should be recognized also as merely an incident in a therapeutic program that would have failed had not the additional aid of immune serum, chemotherapy, transfusions and excellent nursing care been supplied. At the time of operation, the child was seriously ill, but there was no disease of consequence in the lung. The empyema, as well as the pericarditis, was postpneumonic. This sequence is of less serious import than the concurrent appearance of the complication with intra-pulmonary lesions, and may account partially for the favorable outcome. Incidentally, this patient was the third to recover from pneumococcal pericarditis in the hospital records.<sup>8,9</sup> Other cases, even after early and adequate surgical drainage, had always run a discouraging course of continued weakness and increased infection, and after a period of 2 or 3 weeks, the patients died. The presence of empyema as an additional burden has been cited frequently in the literature as highly unfavorable prognostically.

Pericardiotomy was performed in 2 other patients with purulent pneumococcal pericarditis (Cases 1 and 5, Table 1). The drainage of 500 cc of thick pus in Case 1 and 400 cc in Case 5 may have resulted in temporary periods of improvement, but failed to change the progressive course of the disease. Both cases are illustrative of the steady decline in general condition that often typified cases of pneumococcal pericarditis, even after drainage, in the years before chemotherapy and immunotherapy became available. The patients in the remaining 4 cases of pneumococcal pericarditis died without operation.

The pericarditis in 9 cases was due to *Staphy-*

*lococcus aureus* infection, and operation was performed in 3 of these cases, with recovery in 1. Pericardial drainage was without question a lifesaving procedure in this last patient (Case 8), but was postponed until he was almost moribund. The error was largely due to failure to suspect the diagnosis, for the recorded observations indicated the presence of pericardial effusion for many days before it was recognized clinically. Although drainage of the pericardial cavity was adequate in each of the other 2 operated cases (Cases 9 and 11), infection elsewhere was too severe and extensive for a fatal outcome to be prevented. An interesting finding in 1 case was an abscess in the heart muscle, which Nikolaew<sup>10</sup> also considered. Similar myocardial abscesses were discovered in 4 of the 8 fatal staphylococcal infections. In another case (Case 16) worthy of mention in this series, an abscess was found in the left ventricular wall containing thick yellowish pus and presenting against the epicardium but not accompanied by exudate within the pericardial cavity. The occurrence of an actual abscess in the myocardium, without an exudative response in the immediately adjacent pericardium, must be extremely rare.

Three patients died of streptococcal infection, and no operation was performed in this group. One case (Case 19) illustrates the fact that signs of pericardial effusion can at times be produced by a small quantity of fluid, only 100 cc. being found at autopsy. Inability of the pericardium to dilate, owing to preceding inflammatory fixation in association with empyema, is the probable explanation.

In 1 case (Case 20) of influenza-bacillus infection, the patient survived following pericardiectomy.

### DISCUSSION

Even a casual perusal of these cases reveals that suppurative pericarditis finds its most frequent precursors in staphylococcal and streptococcal bacteremia and in pneumonia. Of the 20 cases, 12 were preceded by pneumonitis or pneumonia, 6 by osteomyelitis, 1 by cholecystitis, and 1 by mastoiditis. In the case following cholecystitis (Case 12), the pericardial infection was obviously secondary to perforation of a subphrenic abscess into the pericardium. Ochsner and DeBailey,<sup>11</sup> in reviewing 3608 cases of subphrenic abscesses, found a perforation into the pericardium in 71.

One case of streptococcal pericarditis (Case 19) was probably due to direct extension from a nearby streptococcal abscess in the pleura. In the 2 other cases, the method of metastasis, whether by extension directly, by blood stream or by lymphatic flow, is uncertain. The coexistence of myocardial abscesses in 4 staphylococcal cases and the presence of myocardial abscess in 1 case without concurrent pericarditis indicate the poor prognosis that must be anticipated in staphylococcal pericarditis even after drainage of the pericardium. Such abscesses were not found in infections from other organisms. In none of these cases had the abscess perforated either into the ventricle or into the pericardium, and the case of myocardial abscess without pericarditis suggests that pericardial effusion need not be considered a sequel to abscess. Unfortunately, in no cases in which a myocardial abscess was discovered post mortem had an electrocardiogram been taken. Attention is called particularly to the diagnostic help that might be available from this laboratory method, because in these cases electrocardiographic changes seem to be likely.

Suppurative pericarditis occurred in 12 patients under thirty years of age and in 8 over thirty. Fourteen patients were males, and 6 were females. These figures parallel very closely those derived for age and sex incidence from collected statistics.

### Diagnosis

The difficulty of diagnosis is apparent from the difference of incidence in the figures of the pathologist and the clinician. However, the likeliest cause of this discrepancy is the failure of clinicians to keep in mind the possibility of pericarditis and to seek the signs that suggest it in any case of infection not progressing satisfactorily.

Frequent careful evaluation of the area of cardiac dullness and the character of the heart sounds

is extremely valuable in the early detection of this complication. Muffled heart sounds due to accumulated fluid are a sign that can be supported by x-ray examination, and fluoroscopy is more helpful than film. Not only can diminished or absent pulsations be observed, but alteration in configuration of the cardiac shadow with changes in position can be discovered, as Holmes<sup>12</sup> pointed out; this is a very useful sign.

Kymography furnishes information about the amplitude and character of cardiac pulsations and thus indicates tension within the pericardial sac, but the data from kymography are not always conclusive. The diminution of pulsations is not a sign restricted to pericardial effusions, and Freedman<sup>13</sup> has also observed it in decompensated hearts and in cases of myocardial disease. Berner<sup>14</sup> describes the discrepancy between pulsations of the ventricular wall and those of the aortic knob as being of differential value. In pericarditis, the pulsations of the knob are very distinct, with decrease in movements of the heart itself, whereas in decompensation the weak heart action has an equal effect on the pulsations of both structures. Sufficient observations are not yet available to allow evaluation of this sign.

A number of authors<sup>15-17</sup> have considered the electrocardiographic changes occurring in acute pericarditis. The changes consist in elevation of the RST segments in Leads 1, 2, 3 and 6, and a depression in Leads 4 and 5. These alterations are usually transient, and last not longer than two weeks, after which the most constant change is an inversion of the T waves. These abnormalities can be confused with those of infarction of the myocardium, but when the electrocardiogram is carefully studied in conjunction with the clinical facts it may contribute valuable help. The changes are believed to be due to alterations in the subepicardial muscle layers, and not to the pressure of the exudate, and they are therefore of little value as an actual indication for operation.

Auxiliary signs of great diagnostic value, when present, are a paradoxical pulse, engorged neck veins, an enlarged liver, sacral edema and a pericardial friction rub. The last is transitory. Its presence means much, its absence little. Some degree of cyanosis and respiratory distress is almost constantly observed. The paradoxical pulse is not always easy to feel, but with the help of a blood-pressure cuff the difference during inspiration and expiration can be made more obvious. When the pressure in the cuff is gradually raised, one finds a point where the pulsations during inspiration will just be suppressed.

### Treatment

The mechanical problems of pericardial effusion are different from those encountered in pleural effusion. In the latter, the tendency is to delay operation until the fluid becomes frankly purulent, and until one can expect that enough adhesions have been formed to prevent collapse of the whole lung. The quantity of fluid is, as a rule, not the deciding factor. In pericardial effusion, however, it is mainly the pressure of accumulated fluid that jeopardizes the life of the patient. To control the situation with aspiration is less satisfactory and more dangerous than in pleural effusion. It sometimes happens that the pus is present in a pocket behind the heart, as was true in Case 7 and attempts to aspirate in such conditions will necessarily fail and carry a great risk of injury to the heart. A few cases have been reported in which repeated taps were sufficient to cure even a purulent pericardial effusion,<sup>9, 10</sup> but pericardiotomy is the more reliable procedure. For example, 1 patient (Case 3) was treated by pericardial aspiration because the fulminating progress of the infection and the desperate condition of the patient caused the surgeon to think that pericardiotomy would be a procedure of greater magnitude than the patient could undergo safely. Perhaps so, but it should be noted that 950 cc. of fluid remained in the pericardium after aspiration, and that needle aspiration almost uniformly fails to save the patient.

It is difficult to estimate how much fluid must accumulate in the pericardial cavity to create signs of cardiac tamponade. Slowly developing exudates can reach a quantity of 600 to 700 cc., and sometimes even more, without pressure signs. However, when fluid accumulates rapidly, as with blood in heart wounds, 100 to 200 cc. can give symptoms of severe tamponade. In acute pericarditis, a relatively small amount of fluid can interfere significantly with the circulation. White<sup>18</sup> stresses the engorgement of the veins and enlargement and tenderness of the liver as early signs of pericardial effusion. That this can occur with relatively small amounts of exudate can be seen in 3 cases (Cases 17, 18 and 19), in which only 100 cc. of exudate was present and in which the liver was enlarged and heavy, with the edge well below the costal margin. In cases in which the fluid has not become purulent, one can expect a change every day, and even in these, pericardiotomy is considered by some<sup>6</sup> to be better than waiting, with or without aspiration.

Opening the pericardium is not a difficult procedure, and enough experience has accumulated to show that exposure of the heart to atmospheric

pressure is almost without danger, and certainly less dangerous than exposure to a positive pressure in a closed pericardium. Whether or not a pericardial tap should be performed before operation depends largely on the certainty of diagnosis. The needle is still a blind instrument, and accidents have been reported, however, applied with skill and care, such a tap may yield valuable information. Every effort should be made to avoid infection of the pleura, and for this reason the parasternal approach seems to be the most logical. The technic of pericardiotomy naturally varies with the surgeon. The left parasternal approach used in Case 7 is recommended as simple, safe and effective. Bigger and Bunch<sup>7</sup> also advocate this approach. Moore<sup>19</sup> describes the advantages of a posterolateral dependent drainage, which we believe carries great risk of infecting the left pleural cavity. Gonnard<sup>20</sup> describes median and subcostal epigastric routes of approach, which are satisfactory.

### Prognosis

The prognosis of purulent pericarditis depends largely on the collateral foci of disease, untreated purulent effusion into the pericardium, however, has a 100 per cent mortality. When operation is performed, the chances for recovery increase to about 40 or 50 per cent. From the literature, it seems that pneumococcal pericarditis has a slightly better prognosis, but the present group is too small to warrant any suggestion in this regard.

Fear formerly existed that these patients would develop constrictive pericarditis. This has not happened, however, and probably need not be anticipated unless the effusion is due to tuberculosis. Operation in one case (Case 8) in this series dates back to 1929, and this patient is now in excellent health. A second patient (Case 20) is also in good health three years after operation. A third patient (Case 7) was treated only sixteen months ago and is in excellent condition, but the period of observation is too short to be called an end result.

### Cause of Death

The patients who were not operated on died for various reasons. In many, the bacteremia was overwhelming, and in others the small amount of fluid could scarcely have been responsible for death. In some of the cases, however, early pericardiotomy might have changed the course of events.

### SUMMARY AND CONCLUSION

Three cases of purulent pericarditis are described in which cure was obtained by operation. In the description of a case of purulent pneumococcal pericarditis emphasis is placed on the com-

bination of surgery, immunotherapy and chemotherapy as being responsible for the recovery. Sixteen other cases of suppurative pericarditis are described.

In 5 cases of staphylococcal pericarditis, an abscess was found in the heart muscle; a suggestion is made concerning electrocardiographic studies in such cases.

It is shown that in purulent pericarditis small amounts of fluid, by their rapid accumulation in an unyielding pericardial sac, can give severe signs of heart tamponade.

Problems of diagnosis and treatment of suppurative pericarditis are discussed.

It is concluded that a less pessimistic attitude toward suppurative pericarditis is possible in the light of recent advances in immunology and chemotherapy.

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## ACTIVITIES OF THE BOSTON HEALTH DEPARTMENT\*

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BOSTON

IT is significant to note that men of influence in the early history of Boston gave attention to the prevention and control of disease. Health, history and heroes are bound in one. Our predecessors blazed a trail that has not only kept Boston in the forefront of American municipalities in matters affecting public health, but has left a path that sanitarians of other cities in later years have safely followed.

Many of the men of those early days that we remember through our school histories have their names in the annals of health in this section of the Commonwealth. I have in mind Samuel Fuller, Governor Winslow, the Reverend Cotton Mather and the president of Boston's first Board of Health, Paul Revere. Dr. Samuel Fuller came over on the Mayflower in 1620, and his wife, Bridget Lee, acted as nurse in his professional work in ministering to the colonists.

As early as 1639, Massachusetts provided for the registration of births, deaths and marriages.

In 1647, an act of the legislature against the pollution of Boston Harbor was passed. Statutes that required the isolation of the sick and inter-

esting local regulations adopted in accordance therewith were promulgated in Boston and Salem as early as 1678, so that the attempt to check the spread of communicable diseases is nothing new.

In 1721, the efforts of Zabdiel Boylston and the Reverend Cotton Mather to provide inoculation against smallpox were treated with derision, but Dr. Boylston was later rewarded by being made a fellow of the Royal Society of London.

The Acts of 1799, Chapter 10, empowered "the Town of Boston to choose a Board of Health for removing and preventing nuisances."

In 1816, a law was passed by statute to permit the inhabitants of Boston to choose one able and discreet person from each ward to be a member of the Board of Health.

On December 2, 1872, the mayor was vested with the power to appoint a board of three commissioners to exercise the functions of the Board of Health.

The activities of the Board of Health were originally much more extensive than they are at present; for example, they included the collection of ashes and garbage, which was finally delegated to the Department of Public Works, where it properly belongs.

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In 1894, Boston was the first city in this country or abroad to establish, through its health department, a system of daily medical inspection of children in all public schools. At present, the Health Department prepares daily a list of all the communicable diseases reported for the calendar day, a copy of which is sent to all schools, hospitals and interested institutions in the city. In this way, the School and Health departments cooperate in the proper control of such diseases.

Aside from these functions, which properly belong to the Health Department, there are in Boston certain other phases of health work that in other cities are under the direct supervision of the health departments, but that in Boston are under the control of separate departments. I refer to the registration of births, deaths and marriages, to the hospitalization of diseases of all kinds, particularly communicable diseases and tuberculosis.

The Health Department is composed of the following divisions, as provided by city ordinance: Vital Statistics, Communicable Diseases, Laboratory, Tuberculosis, Child Hygiene and Health Units, Housing and Sanitation, and Food. The Milk Inspection Service is regulated by statute law. The following services have been established within the department: dental, nursing, health education, dairy and abattoir. The department sponsors three WPA projects: an eye conservation program, a nursery school program, carried out on the roofs of the Health Units, and a physical examination program for welfare recipients and WPA workers.

Each of the major divisions is now headed by a deputy commissioner. Since each unit is a decentralized health department, I am desirous of changing this setup, so that there would be only one deputy health commissioner, who would be in charge of the Division of Child Hygiene and Health Units. The rest of the department should be divided into bureaus, with a director in charge of each.

The following are the activities of the major divisions of the Boston Health Department:

*Division of Communicable Diseases* This division deals with the control of reportable diseases, including work incident to lapsed and incorrigible cases of syphilis and gonorrhea and the follow-up of cases for required treatment and hospitalization. Cases of food poisoning are investigated by this division, which also furnishes death certificates in cases in which the medical examiner declines jurisdiction. This division approves licenses to conduct maternity hospitals and homes for the reception of women during pregnancy and in-

vestigates day nurseries. Supervision of the rabies problem by the quarantine of animals is carried out as one of its functions. The veterinarians of this division make annual inspections of cattle, goats, sheep, swine and fowl for the purpose of detecting the presence of contagious disease in animals.

*Laboratory Division* The laboratory provides diagnostic laboratory examinations for diphtheria, tuberculosis, gonorrhea, syphilis, dysentery, malaria, streptococcal infections and Vincent's disease; it performs guinea pig inoculations for the determination of diphtheria virulence and of the presence of tubercle bacilli in body fluids, and it conducts bacteriologic examinations of raw milk, water from swimming pools and beaches, and food. Suitable outfits are provided to physicians, clinics and hospitals for collections from patients of specimens or materials to be submitted to the laboratory for bacteriologic, microscopic or serologic examination. The laboratory is also the distributing center for Boston of the biologicals produced by the Massachusetts Antitoxin and Vaccine Laboratory. The volume of annual performance has increased notably in serologic procedures, owing to the venereal disease program. The pending standardization of all laboratories by the Massachusetts Department of Public Health has resulted in an evaluation study of both Wassermann and Hinton findings in a series of routine blood specimens, with the possibility that the latter method will ultimately be adopted as an accepted routine test. In 1940, about 63,000 examinations were made.

*Tuberculosis Division* The aim of this division is the discovery of cases of tuberculosis and the supervision and disposition to sanatoriums of cases that require treatment. Thirteen diagnostic clinics have been established at strategic points throughout the City. There are twenty-three weekly sessions. The clinics are manned by a group of fifteen physicians, and the attendant service is supplied by the Nursing Service. When hospital disposition is recommended, each case is looked into by the settlement investigator. Boston settled cases are admitted to the Boston Sanatorium, and State settled cases are sent to state sanatoriums. Two pneumothorax clinics are held each week. X-ray films are taken of every patient on the initial visit, and repeat films are often necessary. This X-ray service operates in eight units, and in addition carries out necessary X-ray and fluoroscopic study at the pneumothorax clinics. A weekly nose and throat clinic is held at the Concord Street Unit. Lamp treatments are given to patients with lymph node infections, Wassermann tests are made on all adults, and Von Pirquet skin reaction

tests on all up to seventeen years. In 1940, there were 1245 cases of pulmonary and extrapulmonary tuberculosis (1030 resident and 215 non-resident), and 167 cases of childhood-type tuberculosis. There were 456 deaths from pulmonary and extrapulmonary tuberculosis (419 pulmonary and 37 extrapulmonary). There were 904 admissions to hospitals. In the clinics, there were 22,510 examinations, 6698 x-ray films, 2031 Von Pirquet tests, 1270 Wassermann tests and 639 lamp treatments. There were 3834 pneumothorax treatments.

*Division of Child Hygiene and Health Units.* During the past year, twenty-nine weekly conferences were held in the seventeen baby and pre-school stations located in the Health Units, municipal buildings and settlement houses and staffed by pediatricians from Harvard, Tufts and Boston University medical schools. The medical inspectors participate in the conferences in the Health Units. Six thousand four hundred and eight newborn babies were registered at our clinics last year, as well as 308 children from one to two years of age, and 260 between two and five years. The number of newborn registered represents about 40 per cent of the total births in 1940. Medical inspectors made 224 visits to day nurseries. The physical condition of the children was checked, and vaccinations and immunizations were performed.

*Division of Housing and Sanitation.* The following are some of the activities of this division: routine inspections of tenement houses, three-family houses, private lodging houses and public lodging houses; observation of offensive trades; control of smoke and fume nuisances as related to public health; enforcement of the law relating to surfacing, grading and draining of private alleys; enforcement of building laws relating to public health; supervision of swimming pools, wading pools and beaches, including the taking of samples of water for analysis; rat and vermin control; supervision of conditions along the waterfront; licensing and maintenance of dumps; and survey of plumbing in buildings, including cross connections and inspection of water in dwellings.

*Food Division.* The work done in this division includes control and supervision locally over the sale, production and manufacture of food, drugs and so forth. The Food and Drugs Law, to prevent misbranding of food and drugs, is enforced by this division. Wholesale and retail store inspection, market and bakery inspection, and regular inspection of food establishments requiring licenses are made by inspectors of the division. The control of vehicles used by itinerant peddlers of fish, fruit and vegetables, as well as the fruit and

vegetable terminals and the Boston Fish Pier, comes under it. The City is divided into fourteen districts, and the districts are divided into routes. The inspector is able to cover one route each working day. The "Saturday" market is efficiently handled by this division. The stands and peddlers must pass a rigid examination, which also applies to meat and poultry. Co-operative work is also done with the United States Food and Drug Administration.

*Dental Service.* Dental clinics are held daily in eight health units and two stations from 9 a.m. to 4 p.m. (Saturdays from 9 a.m. to 12 noon). Three days a week are allotted to the children of the public schools, two days to the children of the parochial schools, and Saturday morning is an open clinic for preschool children and emergencies. The attendance during 1940 was 75,523; the number of patients was 38,755; and the number of operations was 127,606.

The regular dental personnel is augmented by the services of five dentists and two hygienists of the WPA.

*Nursing Service.* A policy of generalized nursing has been carried on, and the nurses are assigned to various districts on the basis of need. Under this plan, nursing service is provided for the Communicable Diseases, Child Hygiene and Tuberculosis divisions, including clinic service and necessary home visits. The nurses also give service to parochial schools and day nurseries.

Nurses' visits to cases of communicable diseases in 1940 amounted to 26,710. Visits in the field include follow-up visits on all children attending the twenty-nine weekly conferences held in seventeen different stations throughout the city; and visits to newborn babies to ascertain their need of health supervision were also made. On December 31, 1940, there were 26,727 children under the supervision of our nurses.

Nursing service is given to all but one of the forty-eight parochial schools in Boston, with a school population of 26,275. Five thousand eight hundred and ninety-two visits were made to parochial schools in 1939, and 5210 in 1940.

Nurses assist in the selection and transportation of children to and from the dental clinics.

Twenty-nine day nurseries and nursery schools are given health service by the nurses, and 1286 visits were made to those groups in 1940.

All reported cases of tuberculosis and their contacts are supervised by the nurses until there is some good reason for discontinuing this service. On December 31, 1940, 27,239 patients and contacts representing 8582 families were under the supervision of the nurses. There were 9782 dis-



charges during the year, but there were also 1116 readmissions and 4525 transfers from one district to another. In 1940, the nurses made 123,792 visits to tuberculous patients and their contacts.

Field training is provided for students attending the School of Public Health of Simmons College.

I consider it worth while to correlate the evolution of Boston's public-health program during the last fifty years with the improvement in health conditions that is reflected by the constant reduction of morbidity and mortality, and I shall present some vital statistics from the reports of the Boston Health Department, which furnish a reasonable cross-section of prevalent health and disease conditions in many parts of the United States for the periods enumerated. The mortality rates from specific causes may be considered typical, by and large, for the country as a whole.

Particular attention is called to the encouraging figures that reveal the halving of the general death rate during the last half-century. It is also pleasing to call attention to the tremendous reduction in the tuberculosis death rate and in the deaths from diphtheria, typhoid fever and scarlet fever. Contrasted with this improvement, deaths from heart disease have more than doubled, and those from diabetes and cancer have almost tripled.

What is the comparative picture? In 1940, there were about 50 deaths per 100,000 inhabitants from pulmonary tuberculosis, 0.8 from scarlet fever, 0.3 from diphtheria, and 0.1 from typhoid fever.

In 1890, with a population of approximately 450,000 as contrasted with the present population of about 800,000, there were actually 400 deaths in Boston from diphtheria, as against 2 in 1940; 41 from scarlet fever as against 9; and 155 from typhoid fever as against 1. If the infant death rate prevalent in 1890 were applied to the number of live births in 1940, there would have been 2600 deaths of children under one year of age, as against the 764 that actually occurred.

What have been the results of this half-century of public-health effort in Boston? As already mentioned, the span of life has been materially lengthened; the death rates from all causes have been almost halved; the infant mortality rate has been reduced by 75 per cent, that of tuberculosis by 89 per cent; diphtheria and typhoid have almost been eliminated as causes of death in the community; deaths from scarlet fever have become negligible.

What have been the changing practices that have brought about this remarkable improvement?

Hermann M. Biggs, to whom we owe a great deal for the development of administrative technic in the field of public-health administration, proclaimed that public health was purchasable, and that within reasonable limitations, communities might determine their own death rates. By this statement, he meant in substance that the wise expenditure of adequate funds for the conduct of essential public-health activities would markedly control the prevalence of preventable diseases and deaths from many causes. What are these activities that he had in mind, and what part have they played in influencing the health of the American people? I have already mentioned the significant effect of the application of sound procedures for the sanitation of the environment, the protection of water and milk supplies and the control of communicable diseases. The place of the laboratory as a significant component part of a modern health department has been amply illustrated. The value of immunologic agents has been demonstrated beyond measure as a factor in the prevention of disease.

Very fortunately for organized society, this century has been marked by a number of significant public-health movements, which have required the participation of the individual. The child-hygiene movement, the campaign for the control of tuberculosis, the mental-hygiene movement and the social-hygiene movement, waged by official and voluntary agencies, have stimulated the imagination of the American people, and have resulted in higher standards of individual and community health. Clinics of various types, carrying on the functions in the above-mentioned fields and having for their objectives the prevention and control of disease, have become increasingly utilized by armies of people, who have demonstrated by their reaction the belief that an ounce of prevention is worth a pound of cure.

One should call attention to the significant relation between satisfactory prenatal care and maternal and infant welfare. Studies carried on in Boston have proved that the death rate among expectant mothers receiving adequate prenatal care is about half that among those lacking such medical supervision. Prenatal care has done much to reduce the hazards of the toxemias of pregnancy, injuries at birth and prematurities, and to lower deaths among infants. There is, however, much room for further improvement in reducing deaths occurring during the first month of life.

Both voluntary and official agencies have concerned themselves with the problem of infant, pre-school and school-child health. Milk stations and

baby and preschool clinics have served as the headquarters for the dissemination of information, and for the education of mothers in the very best methods for keeping children well. Among the administrative methods for the conduct of this work has been a co-operative plan developed in Boston, between the Health Department and the Harvard, Tufts and Boston University medical schools, whereby pediatricians from the teaching staffs man the clinics and are reimbursed by the Health Department. Advantage is taken of the presentable opportunity for teaching medical students preventive pediatrics.

It is in the fields of child health and tuberculosis that the public-health nurse has made a lasting contribution. Newborn babies are visited shortly after birth by nurses of the Health Department, and mothers are urged to take their babies either to their own family doctor or to the clinic for periodic medical supervision. Here, children are examined, vaccinated against smallpox, and immunized against diphtheria. Breast feeding is stressed, and whenever possible the use of pasteurized milk and the preparation of the proper formulas are taught. When children arrive at the preschool age, the so-called "neglected age," every effort is made to maintain the continued interest of the parents in the physical and mental health of the child. There is, however, room for much further progress in this age group.

One is familiar with the frequency with which faulty teeth, defective vision, defective hearing, malnutrition, faulty posture, functional or organic heart disease and occasionally tuberculosis are found among the school-child population. Large sums are being spent in the United States for the medical inspection of schools and physical examinations for the discovery of remediable defects. Emphasis should be placed on the value of increasing efforts for the correction of defects found. An example of excellent service in this field is the program carried on by Dr. James A. Keenan, his school physicians and nurses in the Boston Public Schools; the Health Department assumes the responsibility for medical inspection in the parochial schools.

The care of the mouth and primary teeth is receiving fitting recognition. It is hoped that what is being done for children today in the way of preventive dental care may bring about higher standards of dental health for the American people. An outstanding example of municipal interest in this field is the program of the Health Department, whereby a corps of approximately

twenty dentists and ten hygienists of the Forsyth Dental Infirmary carry on prophylactic dental service in the Health Units. This personnel is reimbursed from tax funds.

Attention is being given to the subject of proper nutrition as a factor in normal growth and development, to the eradication of faulty food habits and to the establishment of proper and well-balanced diets.

The attack against tuberculosis represented what may be termed the second important public-health effort at the beginning of the present century. Case-finding, the isolation of the infected person, the rounding up of contacts who have been exposed, occupational adjustments and pneumothorax are all a part of the modern campaign for coping with this problem. Today, every health department of appreciable significance either maintains, or sees to it, that there exist in the community adequate facilities for tuberculosis control.

For a number of years, the subject of the control of venereal diseases was approached, except in rare cases, with much diffidence and hesitation. Gonorrhea and syphilis represent an important public-health problem. Stimulated by the efforts of the National Society for Social Hygiene, and more recently by the vigorous challenging efforts of Surgeon General Thomas Parran, and with the assistance of federal funds, a worth-while program is constantly making further progress. The Massachusetts Department of Public Health, with the aid of the above-mentioned funds, not only assists in the maintenance of a number of venereal-disease clinics, but stimulates the upholding of adequate standards. Of particular significance is the organization of facilities for rounding up the lapsed cases.

During the present century, there has been an increasing recognition of the relation of housing to health and the control of disease. It has been recognized that adequate light, air and ventilation and the avoidance of overcrowding are minimum requirements in the field of human needs.

There is a need for an increased recognition by those responsible for community health of the problems of mental hygiene and mental disease. A ray of hope is offered by the expansion of the child-guidance clinics conducted under official or voluntary auspices, which deal with the problem of faulty habits in children and the need for the improvement of the environment to which the child is exposed. Certainly, the tragically high prevalence of mental disease should focus attention on the need of more prevention.

Vigilant health officers appreciate the value of an understanding by the public of the functions and objectives of the Health Department. Healthful living needs interpreting in simple, understandable language. The spoken word in the clinic, in the lecture hall and over the radio, and the visit of the public-health nurse can be opportunely utilized for educational health propaganda. The leaflet, the poster, the pamphlet may all serve the useful purpose of making people more health-minded. Here and there, health educators employed by health departments are living examples of changes in public-health practice from police methods to education.

As deaths from preventable causes have been lessened and the average span of life increased, many persons are living to middle and later life, with a consequent increase of the diseases prevalent in the older groups. Among these illnesses are cardiovascular disease, cancer and diabetes. This newer public-health problem should be the concern of the health officer. Although this does not imply that he must necessarily conduct medical activities for the treatment of these diseases, it is his obligation both to educate the public in methods for their control and to see that there are in his community an organized medical profession, clinics and hospitals to cope with these problems.

The health officer today integrates the efforts of administration—the findings of the statistician, the medical inspector, the public-health nurse, the milk, food and sanitary inspector, the laboratory technician and the school physician—with those of the representatives of the voluntary health agencies. Today, in cities of varying size, health services are frequently conducted on a district basis. Radiating from the health centers, which were founded to bring together under one roof in a spirit of service and of team play all concerned with the problem of health and welfare, these services attempt to present a united front against sickness and death.

Statistical figures that corroborate the assumption that improvements in health result from changes in public-health practices tell but a part of the story. Even more can be done. There are still too many deaths from preventable causes. Health workers can add more years to the span of life and improve the span of health, since the knowledge and methods at their disposal possess rich, lifesaving values. They must create, by education and by the conduct of adequate programs, a greater desire on the part of everyone for life's most treasured possession—optimum physical and mental health.

Since I have been health commissioner, I have been very fortunate because of the establishment of the Advisory Council, composed of leaders in the fields of public health and medicine and of representatives from the voluntary agencies, under the able leadership of your president, Dr. George C. Shattuck. Each of these leaders is to make a special study of a division or service of the Health Department, and will make recommendations that will result, I am sure, not only in improvement of efficiency, but also in raising the standard of performance. This council has had two meetings so far, and I can honestly report a true spirit of co-operation and progress in the right direction.

In the Laboratory Division, we are making some special studies in whooping cough, and also working out a new method for gonococcus culture and diagnosis as a part of the program for the control of venereal disease. In the Milk Inspection Service, we have succeeded in obtaining the co-operation of all the milk companies supplying Boston, so that by July 1 of this year, we should have 100 per cent pasteurization of the Boston milk supply.

In the interest of national defense, the Boston Health Department, through its Laboratory Division, has recently co-operated with the Government in performing thousands of blood tests for selectees and the National Guard. In conjunction with the Massachusetts Department of Public Health, the Tuberculosis Division has x-rayed several hundred selectees. This year, I earnestly hope to set up, with the co-operation of the State Department of Public Health and with the help of federal funds, a greatly improved and enlarged health-education program, as well as a much more comprehensive program for the control of venereal disease.

I compliment all the private and voluntary agencies in the City of Boston, many of which are housed in the Health Units, for I honestly believe that in no other city is the relation between the Health Department and these agencies more pleasant and more harmonious.

It would be in poor taste for me to make any preposterous claims for the Boston Health Department, but I should like to emphasize that I know of no perfect performance by any health department, and I am of the sincere conviction that the combined performance of the Boston Health Department and the voluntary health agencies compares favorably with that of any other large city in the country.

## SPONTANEOUS MEDIASTINAL EMPHYSEMA\*

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SPONTANEOUS mediastinal emphysema should always be considered in the differential diagnosis of pain in the chest, because if the diagnosis is missed, a grave prognosis may be given for a benign condition.

The history of the pain associated with spontaneous mediastinal emphysema may well be consistent with coronary thrombosis, pericarditis, ruptured or dissecting aneurysm, mediastinitis, pulmonary embolism and spontaneous pneumothorax.

The syndrome may occur at any age, usually in a healthy person, with or without exertion. The onset is frequently alarming and dramatic, with sudden precordial or substernal pain, shortness of breath and cyanosis. The pain may be slight or quite severe, and it may be necessary for the patient to remain in one position for relief. He may feel or hear a peculiar grinding or crunching in his chest with each heart beat, with swallowing or with change in position. The pain may gradually subside within a few hours or may persist with exacerbations and remissions for a variable period. The patient may recover completely, only to have the same train of symptoms recur after a few weeks, months or years.

On physical examination, the patient usually appears comfortable except for the pain. The temperature, as a rule, is normal, with normal or slightly elevated pulse and respirations. Dyspnea and cyanosis are sometimes present. Certain important physical signs are found. Dullness to percussion over the left border of the heart is diminished or absent. Bubbling, crunching and gurgling to-and-fro sounds are heard over the precordium. These sounds are altered by change in position, and may cease with the disappearance of pain. Signs of pneumothorax may be found, but the pneumothorax is frequently so small that changes are not apparent on physical examination. Occasionally, air may appear under the skin of the neck or above the clavicles.

The diseases that are confused with spontaneous mediastinal emphysema are, as a rule, readily differentiated. The history alone may be sufficient to make the diagnosis, particularly if the patient is conscious of these gurgling, crunching sounds, with relief on change in position. The presence

of air in the subcutaneous tissues of the neck or periclavicular regions is helpful. Previous adjacent operation may be the cause of mediastinitis or pericarditis, and infection or operation at a distance, by subsequent thrombophlebitis, may produce pulmonary embolism. Small infected emboli may produce mediastinitis, with or without concomitant pulmonary infarction. The presence of fever and leukocytosis and characteristic electrocardiograms serve to differentiate coronary thrombosis and pericarditis. X-ray examination may be essential, however, if obvious signs are not brought out on the first examination. Subfascial emphysema, often present after artificial pneumothorax, need not be confusing.

Hamman<sup>1, 2</sup> is credited with calling attention to the uncommon syndrome that bears his name. He was able to prove some of his cases either by x-ray or by subsequent clinical course, in addition to the characteristics mentioned above. Morey and Sosman<sup>3</sup> reported a case in a young man in which there was a small pneumothorax. They stated that the disease may occur as a result of coughing, in asthmatics, in labor, after trauma and operation, and following artificial pneumothorax. They mentioned the possible necessity of incising the neck to release the accumulated air. By overdistending the lungs of cats and other animals with a truncated catheter, Macklin<sup>4</sup> has shown that air dissects into the perivascular sheaths and travels along these sheaths to the mediastinum, thus producing a mediastinal pneumothorax. Clinically, this condition may occur when the alveoli are subjected to abnormal pressures in the closed method of anesthesia, in infection with bronchial or bronchiolar obstruction, and in pathologic conditions of the heart and great vessels. The dissection of air may extend to the opposite lung, to the abdomen (to produce a pneumoretroperitoneum), to the neck and to the periclavicular regions. Scott,<sup>5</sup> Faulkner and Wagner<sup>6</sup> and Caldwell<sup>7</sup> have written on the subject. Caldwell mentioned a traumatic case due to a stab wound, in which the patient was found to have typical signs the day after the accident.

## CASE REPORTS

CASE 1. J. C., a 33-year-old man, was quite well until April 15, 1940, when, while walking, he was seized by a gripping pain in the midscapular region that radiated

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around to the precordium, up to the left shoulder and, finally, down the left arm to the wrist. The patient was unable to get his breath, felt weak, and was forced to sit down. He dared not move at the time for fear of aggravating the pain and, indeed, feared that he was going to die. The pain lasted about 3 hours, at the end of which he was brought into the hospital. He remembered having had a somewhat similar pain 12 years previously.

Physical examination showed an asthenic young man lying quietly. He was apprehensive. The face was flushed, the tongue was tremulous, and the trachea was in the midline. The left chest was somewhat full anteriorly. Expansion was equal, and both lung fields were resonant. Breath sounds were normal. The left border of the heart was 9.5 cm from the midsternal line. The heart rate was regular and rhythmic and a faint systolic murmur was heard at the apex, a faint transient grating sound was heard in the tricuspid area.

The blood pressure was 140/80, the temperature 97.8°F, the pulse 65, and the respirations 22.

At the time of examination, the patient was thought to have a coronary occlusion. He continued to have substernal pain off and on for 2 days. On the 3rd hospital day, the patient complained of a to-and-fro thumping noise. The sound was easily heard at a distance of several feet from the chest wall. When a stethoscope was placed on the precordium, very loud crunching bubbling sounds were heard. The sounds altered markedly with change in position, and were best heard on the left side. The same phenomenal sounds were heard at a later time. In the course of a few hours, the sounds disappeared permanently.

Three electrocardiograms at intervals of several days were normal. Westergren sedimentation rates at 3-day intervals were 1, 6, 8, 6, 4 and 5 mm at the end of 1 hour. The white-cell count was never over 6800. Serologic tests were negative. The nonprotein nitrogen was 26 mg per 100 cc. A foot x-ray film of the chest was within normal limits.

The patient was followed at monthly intervals for a year and had no recurrence. Repeated electrocardiograms were normal.

Although no x-ray evidence of a pneumothorax was found, it was concluded that the signs described above were so typical as to furnish unmistakable evidence of mediastinal emphysema. Furthermore, the clinical diagnosis was certainly supported by laboratory studies.

CASE 2 F.M., a 22-year-old man, was well until August 31, 1940, when, while walking along the street, he felt a stabbing precordial and left-sided chest pain. He became short of breath and had to sit down for relief.

He was brought to the hospital. Following arrival, he remained fairly comfortable.

The patient seemed rather frightened but felt generally well. His color was good. The trachea was questionably deviated to the right. Expansion of the thorax was equal. The lung fields were resonant. Breath sounds were slightly diminished high in the left axilla and at the left apex posteriorly. The left border of the heart was 8 cm from the midline in the 5th interspace. With the patient in the recumbent position, the heart sounds were regular and rhythmic, with a very faint scratching sound characteristic of a friction rub. However, when he was turned on the left side, loud, crunching, bubbling, gurgling, to-and-fro sounds were heard and were audible to the patient. The sounds were easily heard a foot and a half from the chest wall without the aid of a stethoscope. In addition, the patient noticed some pain when he was placed on the left side.

The blood pressure was 120/80, the temperature 98°F, the pulse 70, and the respirations 20.

A 7 foot chest plate revealed a small pneumothorax at the left apex, the pleural surfaces were separated at the apex by 1.3 cm. No air was seen in the soft tissues. An electrocardiogram was normal, and other laboratory data were within normal limits.

The patient remained quite comfortable after the first few hours in the hospital. Twelve hours after admission, no unusual cardiac sounds could be made out. He was seen in the Outpatient Department a month after the episode and reported that he had been well.

#### SUMMARY

A brief discussion of spontaneous mediastinal emphysema is accompanied by a short review of pertinent clinical and experimental literature, and 2 cases are reported.

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## MEDICAL PROGRESS

### OVULATION

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UNTIL very recently, medical students were taught that at birth the fetal ovary contained all the primitive follicles that would ever appear, that thenceforth no more eggs would be developed from the germinal epithelium. This view is no longer tenable. Studies of Allen and Creadick<sup>1,2</sup> on the mature mouse and of Evans and Swezy<sup>3</sup> on the rat, guinea pig, dog, cat and man show that from birth to the climacteric, cell division in the germinal epithelium constantly produces new cells, which move centrally into the stroma. In man, these are, before migration, differentiated into ova and follicle cells. This proliferation of germinal cells depends apparently on an intrinsic urge to grow that is characteristic of all living tissue. The primitive follicles, with a similar growth potential, increase in size; and, including those of early embryonic origin, they secrete estrogen, which directs the secondary sex development. Even before birth and continuing until puberty, some follicles enlarge to the appreciable diameter of several millimeters, while estrogen production increases. All the follicles, however, stop short of complete growth. Around each, the theca interna, which is clearly derived from the ovarian stroma, remains rudimentary, and so far as is known, except in very rare and abnormal instances, the nucleus of the ovum does not divide, nor does the ovum escape. During prepubertal life, there is a constant regression of the larger follicles and their ova, as well as a growth of the smaller and younger ones.

With puberty comes a change in the secretion of the pituitary gland which results in a reduction of the rate of ovogenesis.<sup>4,5</sup> Of greater import, however, is the advanced growth that occurs in those ova and follicles already present. Fevold, Hisaw and Leonard<sup>6</sup> have separated the maturity principle from the anterior lobe into a follicle-stimulating hormone and a luteinizing hormone. By action of the former, many follicles increase in size, and the production of estrogen mounts; by action of the latter, the theca interna surrounding the granulosa cells develops into a luteal layer, which contains fat droplets and which

undoubtedly secretes progesterin. When this occurs, the ovum, also in response to these two hormones, possibly assisted by a thyroid secretion, undergoes its first reduction division and extrudes the first polar body.<sup>7</sup> Ordinarily, in the human female, such stimulus from the pituitary gland is sufficient for, or is accepted by, only one of the many ova in both ovaries. As this one ovum matures, its growing follicle, now encased in an active luteinizing theca interna, migrates to the surface of the ovary. Secretion of follicular fluid continues; intrafollicular pressure rises.<sup>8-10</sup> The cortical covering of the follicle suffers pressure ischemia at one point; the theca interna bulges through as a small nipple, and finally the thinned-out wall of the follicle ruptures. The follicular fluid escapes, washing out the cumulus and its contained ovum.<sup>11</sup> Thus, ovulation is accomplished.

With the extrusion of the ovum, and the evulsion of some, if not all, of the granulosa layer, the theca interna closes the ostium and, as some believe, in conjunction with the remaining granulosa tissue, develops rapidly into the new master gland, the corpus luteum. This potent gland of limited life, in addition to estrogen, secretes progesterin, which is chemically somewhat similar to estrogen but pharmacologically quite different from it.

Before the rupture of a chosen follicle is due,—that is, during the preovulatory phase of follicular growth,—many grossly discernible follicles in one or both ovaries contain normal ova surrounded by proliferating granulosa cells. This doubtless indicates that the enclosed ova are also progressing toward maturation. Ordinarily, however, only one apparently forms a polar body and is liberated. After this event, the proportion of degenerating and atretic ova increases.<sup>12,13</sup> Pincus<sup>14</sup> states that in mammals "mature ova retained in the ovary at the time of ovulation ordinarily degenerate." Meiotic division has been reported in a human follicular ovum at a time when a secretory endometrium gave evidence of corpus-luteum activity.<sup>15</sup> This, however, may represent an early step in the breakdown of the egg, since, as Pincus<sup>16</sup> states, "the atresia of ovarian eggs is often initiated by the formation of a maturation spindle."

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Ova that do grow following ovulation regress before the maturation stimulus from the pituitary comes again after menstruation.

It is clinically very significant that during the activity of the luteal tissue, which begins shortly before ovulation,<sup>17</sup> no further normal maturation of other ova takes place. When the corpus luteum regresses and progesterin diminishes, a new crop of partially developed ova and follicles begins advancing toward maturity.

To clarify some later considerations, it is well to review the physiology of menstruation. Estrogen from the follicles stimulates the endometrium to grow—to proliferate. The stroma becomes thicker; the arterioles increase in size, and the capillaries in complexity; the glands become larger and more numerous. The histologic picture of both the glands and the stroma is well known and characteristic.<sup>18-20</sup> At the time in the menstrual cycle when progesterin, elaborated by the corpus luteum, becomes effective, the proliferated endometrium is said to become "secretory": it "functions." This secreting or functioning mucosa likewise has a histologic appearance that, conversely, specifically indicates progesterin activity. The human corpus luteum ordinarily functions only just before and for two weeks after ovulation. Enough progesterin to elicit the cytologic picture of beginning secretion in the endometrium is usually produced during about the second twenty-four hours after ovulation. The cytology of this continuing functional phase exhibits a well-known orderly and progressive series of stages each of which individually possesses distinguishing features. Thus, by examination of a biopsy specimen and recognition of any one of the stages, the observer may estimate how long progesterin has been acting, and therefore how long the corpus luteum has been present. And so, by the endometrium, one may estimate when ovulation took place.

If conception and implantation have not occurred, the activity of the corpus luteum finally ceases, and the potentiality to bleed, which has been developed in the endometrium by estrogen and kept from expression by progesterin, is released by withdrawal of the progesterin.<sup>21</sup> As a result, blood is extravasated into the tissue. This disintegrates and menstruation ensues.<sup>22</sup>

#### TESTS FOR OVULATION

Are there any means, besides endometrial biopsy, by which one can tell whether and when ovulation, that event of such potentially tremendous import to the individual and to society, takes

place? Of the numerous tests that have been proposed, the following are the most popular ones.

#### Mittelschmerz

Some women experience with ovulation a momentary lancinating pain in either lower quadrant, usually superimposed on preceding dull discomfort of several hours or even days. Wharton and Henriksen<sup>23</sup> state that the pain is usually so mild as to be undetectable until after educated attention has been directed to it. Ito<sup>24</sup> reported that 70 per cent of a group of female medical students and physicians were able to detect ovulation by their subjective symptoms, whereas only 40 per cent of nurses in the series studied were able to do so.

In Boston, surely not more than 15 per cent of women receive such information. This discrepancy is presumably not due to territorial favoritism on the part of Nature, but may indicate a lack of particular education and attentiveness. Doubtless, many hitherto heedless women could be trained. Although the information is very useful, distressful confusion might arise in many emotional females from intensively applied abdominal introspection. However, the method has merit and should be more commonly applied.

#### Intermenstrual Bleeding

In 20 per cent of the cases studied by Wharton and Henriksen,<sup>23</sup> the *Mittelschmerz* was accompanied by intermenstrual bleeding profuse enough to require protection. More commonly, bleeding at the midcycle arises unassociated with pain. The flow varies considerably in amount. Sometimes, it appears merely as a pink or brownish stain in mucus. In his study of intermenstrual bleeding in macaques, Hartman<sup>25</sup> found that, when bleeding occurred at ovulation time, it was usually in microscopic amounts. Wharton and Henriksen microscopically examined the vaginal washings of 5 women with no gross bleeding and found blood in all. Papanicolaou<sup>26</sup> also noted that almost 24 per cent of vaginal smears taken on the fourteenth day contained microscopic traces of blood. This flow at ovulation time is sufficiently gross to attract the attention of probably less than 5 per cent of women.

#### Biochemical Study

In many laboratories, efforts are being made to measure in blood and in urine the amounts of female sex hormone—the combined estrogens. When the values obtained for estrogen content of urine for several unit periods of twenty-four or forty-eight hours throughout the cycle are plotted

against time, curves are obtained that are considered typical of the ovulatory cycle. Although the absolute amounts of total estrogen in the urine may vary in assays by different chemists, there is a semblance of uniformity in the curves. Those of Gustavson et al.<sup>27</sup> do not reflect the findings of Smith and Smith<sup>28</sup> that a marked peak is demonstrable twelve or thirteen days before the next catamenia, but their published curves do show peaks between the fourth and twenty-first days before menstruation. Werner<sup>29</sup> also comments on the appearance of an estrogen peak at about the middle of the cycle, and its reduplication a few days later. Furthermore, Gustavson states that in every case the estrin excretion falls to zero at or very shortly preceding the next ensuing menstrual period.

Kurzrok, Kirkman and Creelman<sup>30</sup> reported the sudden appearance of the follicle-stimulating hormone (prolan A) in the urine, usually about the middle of the menstrual cycle. Using a more sensitive method, D'Amour<sup>31</sup> and Werner<sup>29</sup> obtained values for urinary gonadotropin throughout the cycle. In the majority of their cases, the resulting curves showed a peak about sixteen to twelve days before the succeeding menstruation.

Another biochemical measurement—that of the excretion in the urine of pregnanediol, a breakdown product of progesterin—is also informative.<sup>32</sup> When pregnanediol first appears during the cycle, one may assume that the corpus luteum is in the ascendancy, since, in the absence of conception, progesterin (containing progesterone) comes only from the corpus luteum.

Collection and delivery of many specimens of urine or blood entail much inconvenience, and the chemical analysis requires much time and expense, as well as a rare degree of skill. The determination of hormone content is therefore still to be considered a research method, and is of relatively little value for the clinical problem of detecting ovulation.

### *Basal Body Temperature*

Rubenstein<sup>33</sup> proposes that, in normal women during the childbearing period, rectal temperatures taken at the same time each day and under standard basal conditions vary characteristically during the menstrual cycle, and if plotted against time describe a specific curve informative of ovulation. His proof that the selected portion of the curve truly denotes ovulation depends to some extent on a few pregnancies that have followed coitus at this time but, more especially, on a change in the quality of epithelial cells recovered from the depths of the vagina. This change he

sees occurring synchronously with what he considers to be characteristic variations in temperature. It would seem easy for patients to read and record their rectal temperatures at the same hour every day, but I must confess my inability to recognize in more than one of the few curves obtained from my patients the particular series of variations of from less than 0.5 to 1°F. or slightly more that are taken to indicate ovulation. Since the accuracy with which patients can determine and record rectal temperatures at particular times under particular conditions is questionable, and especially because variations of so slight a degree are incident to so many conditions besides ovulation, this method does not appear to be a reliable one for determining the time of ovulation.

### *Vaginal Smears*

In 1917, Stockard and Papanicolaou<sup>34</sup> presented their pioneer work relating changes in the vaginal epithelium of guinea pigs to the estrous cycle. On this groundwork, a very large part of modern sex endocrinology has been built. In 1933, Papanicolaou<sup>26</sup> described a method of obtaining the vaginal desquamate of women and of staining a spread of the cells. He designated the varying qualities of the stained smear as indicative of definite sequential phases in the ovulatory cycle of the human female. Many ardent workers have used his method and learned much about the effect of estrogen on the vaginal epithelium. From smears, one can usually detect the failure of the ovaries to form many active follicles, as in some cases of amenorrhea and in the menopause, and likewise discover the presence of many follicles secreting estrogen in the ovulating woman. In smears, one also detects the effect of the relatively enormous amount of estrogen secreted by the placenta in pregnancy. Few, however, and I am not one of them, have been able, with Papanicolaou's stain, to see changes specifically indicative of ovulation on or about the day it occurs. Hence, as a method of detecting ovulation, the vaginal smear is yet of very limited, if any, clinical value. Great conservatism in its use is also advised by other investigators.<sup>35, 36</sup>

A new method of staining vaginal smears recently described by Shorr<sup>37</sup> may prove helpful. By its use, one can demonstrate ovulatory changes in the macaque.<sup>38</sup> In the macaque, however, ovulation is associated with exceedingly gross alterations in the tissues of the vagina and vulva, which are only very faintly simulated in the human female. It seems to me that variations in the vaginal desquamates during the human cycle are equally slight.



### Biopotentials

In 1935, Burr and his collaborators<sup>39</sup> reported that, with ovulation in the rabbit, there was a demonstrable increase in the difference in potential between two electrodes, one placed above the symphysis and the other in the vagina. Reboul, Friedgood and Davis<sup>40</sup> repeated Burr's experiment and furthermore discovered by direct observation that this change in biopotentials was synchronous with ovulation. In 1937, Burr and his associates<sup>41</sup> reported a similar phenomenon in one woman. This was also demonstrated in one case in my clinic.<sup>42</sup> Rock, Reboul and Snodgrass<sup>43</sup> later reported changes in difference of potential at the time of ovulation in 9 other women, but because 3 of these were found at operation to be only on the verge of ovulation, it was proposed that the recorded increase in the difference of potential was merely associated in some way with ovulation. This conservatism was supported by Rogers's<sup>41</sup> observation that a similar change in biopotentials was obtained in the spayed rat during the last day of estrogen-induced estrus. However, in 1940, Barton<sup>45</sup> suggested that wide changes in the difference of potentials between two index fingers indicated ovulation. Furthermore, she concluded from her data that ovulation might occur at any time during the cycle, and sometimes twice in the same cycle. Impressed by the facts that the abdominovaginal sign was obtained sometimes before and sometimes with or after ovulation, that its polarity was inconstant and, particularly, that there were wide variations in the magnitude and duration of the change in difference of potential, Snodgrass<sup>46</sup> attempted to discover something more about the cause of these potentials. Very significantly, he found that the potentials between fingers were affected proportionately by changes in the environmental temperature of one finger. It was also noted that daily differences in potentials between fingers were very probably influenced by atmospheric temperature and humidity affecting the body as a whole.<sup>46, 47</sup> Finally, of great clinical value is the fact that, contrary to Barton's findings, rather intensive study in my clinic proves that the so-called "finger-to-finger potentials" have no relation whatever to ovulation. As the complete report of our researches has not yet been published,<sup>48</sup> I take this opportunity to say that, like basal body temperatures and vaginal smears, biopotentials may be affected by ovulation but not in such a critically peculiar way as to indicate ovulation, and therefore, like the other methods, cannot be used clinically to detect this significant event.

### Endometrial Biopsy

Is there any dependable means of telling whether or not ovulation takes place? I referred above to the fact that estrogen alone causes a proliferation of the endometrium that results in a characteristic cytologic appearance, and that, when progesterin comes into action, function or secretion is evoked in the proliferated tissue, again with a typical cell picture in the glands and later in the stroma. By aspiration into a small suction curet of a fragment of endometrium before an expected catamenia, one may, after section and staining, determine whether or not progesterin has been elaborated in the ovary.<sup>20, 49, 50</sup> If the signs are there, one may deduce the presence of a corpus luteum, and hence that ovulation has taken place. At present, endometrial biopsy is the best clinical test for the occurrence of ovulation.

### TIME OF OVULATION

So regular are the successive changes in the functioning endometrium as the secretion of progesterin waxes with the growth of the corpus luteum and wanes with its regression, that one may discover not only *if* ovulation occurs but also approximately *when* it occurs.

In the first years of this century, the prevailing view among biologists was that the egg was released about the time of menstruation.<sup>51-53</sup> Recently, Barton<sup>15</sup> deduced from observations of finger-to-finger potentials, which I consider not at all indicative of ovulation, that in 18 per cent of them (24 per cent in a smaller series<sup>64</sup>), it occurred in the midcycle, but in the rest at any time in the cycle, even during menstruation. Rubenstein<sup>33</sup> believes that he has demonstrated by changes in basal body temperatures and vaginal smears, both of which I consider misleading or uninformative, that ovulation usually takes place near the midcycle, but may occur at other times, even during the menses. By correlation of observations of the ovaries at laparotomy with the anticipated dates of catamenia, Ogino,<sup>55</sup> on the other hand, convinced himself that ovulation occurs between the sixteenth and twelfth days before menstruation; and Knaus,<sup>56</sup> by observation of the myometrial response to posterior pituitary extract as affected by progesterin, concluded that it takes place on the fifteenth day preceding the onset of the menses. By correlation of the age of the corpus luteum (as evidenced in the stage of endometrial functioning detected by biopsy) with the date of the subsequent menstruation, in more than 400 biopsies in my clinic, we have, in about 75 per cent of these, placed maturation of the ovum

and probable ovulation at the sixteenth to the twelfth day before the onset of menstruation. At present, by more accurate reading of the endometrial section, in about 90 per cent of cases it is possible to foretell within about two days when, in the absence of pregnancy, menstruation will occur. The calculations are based on the assumption that the corpus luteum functions for about two weeks, and the accuracy of prophecy bespeaks the soundness of the theory. In the few remaining cases, the question may well arise whether or not something is wrong with the hormonal control of endometrial bleeding, rather than whether or not ovulation takes place at the time indicated by the degree of progestin effect.

By applying this proposition to the prevention of pregnancy, we believe we have proved, as many others have, that ovulation normally occurs about fourteen days before the succeeding menstruation. Allowing three days for the effectiveness of spermatozoa and an admittedly long period of three days for the susceptibility of the egg to fertilization, we have reduced the fertility rate among 109 women from 90 pregnancies per 100 person-exposure years to only 4.<sup>57</sup> The proposition that the ovum is freed on about the fourteenth day before menstruation cannot be far wrong when coitus is freely practiced at other times by 109 very fertile women and so very few of them become pregnant. The exceptions are properly explained by the impossibility of always accurately placing the next menstruation.

It should be noted that I do not say that ovulation occurs about the fourteenth day of the cycle. From our biopsy studies, we are convinced that in cycles varying in length from the ordinary twenty-seven days, that is, in cycles that terminate with menstruation on the twenty-eighth day, the variable is in the follicular (proliferative) phase — the period following catamenia. The luteal or secretory phase is relatively constant, varying from 12 to 16 days. On the basis of controlled mating experiments in the chimpanzee, Elder<sup>58</sup> in like manner emphasized the importance of taking into account the length of the cycle when estimating ovulation time: that is, he found ovulation to take place earlier in short cycles than in long ones.

#### FAILURE OF OVULATION

Since long before the suggestion in 1908 by Hitschmann and Adler<sup>59</sup> that the ovary might have a causal relation to cyclic changes in the endometrium, the occurrence of uterine flow has been regarded as a sign that ovulation had taken place, and amenorrhea has been considered evidence of its failure. It is now known that neither of

these views is strictly tenable. In only 1 among more than 400 biopsies, have I seen evidence of a corpus luteum, bespeaking ovulation, in a patient who did not, in the absence of pregnancy, subsequently menstruate. Such a rarity offers only a dangerous clinical pitfall. A diagnosis of ovulation during amenorrhea must never be made without clear proof.

Likewise, in about 10 per cent of 392 infertile women, we<sup>60</sup> found evidence of anovulatory menstruation. In 50 per cent of this group of anovulatory patients (or about 5 per cent of the entire group of sterile women studied), such evidence was obtained by more than one biopsy—that is, flow from an endometrium still in the proliferative stage. This phase, as I have pointed out, indicates the presence in the ovaries only of active follicles and not of a functioning corpus luteum. The absence of this gland accounts for the fact that anovulatory menstruation occurs at widely varying intervals and not with the usually constant periodicity of the flow that follows the action and regression of a corpus luteum. Not only do normal postovulatory menstrual periods commonly recur at fairly constant intervals, but such catamenia are similar in the duration, quantity and quality of flow. On the contrary, the flowing that occurs with failure to ovulate is very variable in these details. For this reason, I think the term "aperiodomenorrhea," meaning irregular, immeasurable menstruation, is proper. I have no accurate figures, but I should guess that, in women between sixteen and forty-five years of age, failure of ovulation is reflected in aperiodomenorrhea at least three times as often as it is in amenorrhea. The latter, like the symptomatic syndrome of the menopause, usually indicates the failure not only of ovulation but also of appreciable growth of all but perhaps a very few follicles.

#### INDUCTION OF OVULATION

The means to stimulate ovulation should logically have reference to the normal physiologic activators of ovular and follicular maturation. Since comparatively little is known of the physiology of human ovulation, it is not surprising that efforts to evoke this phenomenon in women who suffer its failure are often in vain. Even when ovulation does follow certain procedures, one is usually unable accurately to determine the successful underlying process.

#### *Thyroid Therapy*

Results from thyroid medication are a good example of inexplicable consequent ovulation. In a small proportion of cases (perhaps not more than

5 per cent), ovulation follows the administration of as little as 1 gr. of the dried gland daily, even in patients whose basal metabolic rates are normal. Pincus<sup>61</sup> states that the thyroid may promote oogenesis to a certain extent. Salter<sup>62</sup> cites evidence indicating that the thyroid gland is related to ova production in the bird.

### *Diet and Hygiene*

Empirically, likewise, the relief is called for of anemia and the probably associated occult deficiencies of vitamins or minerals when ovulation fails, whether or not to the extent of amenorrhea. This should be the first attack on the problem. Although the condition is not so serious as the subclinical pellagra considered by Mc Lester,<sup>63</sup> one should remember his advice that "the physician who would treat deficiency diseases cannot afford to be timid." It is therefore well to give relatively large doses, especially of the vitamins, when one is working on the theory that they may be missing. Physical and mental hygiene should not be neglected. Exercise, rest and equanimity are beneficial. Although the relation between emotional tone and ovarian function is not clearly understood, it is frequently apparent, and an effort should be made to resolve what mental conflicts one can discover.

### *Hormones*

During the last few years, endocrinologic attacks on anovulation in the human female have been suggested by attempts on laboratory animals that were relatively successful.

**Chorion hormone** Experiments were undertaken with the chorion or anterior pituitary like hormone, extracted from the urine of pregnancy. This evokes maturation and ovulation in even the immature rat and mouse, and so surely elicits these phenomena in the isolated rabbit doe as to establish the dependable Friedman test for human pregnancy. This hormone, however, under any of its many pharmaceutical titles, completely fails to produce the desired result in human patients. Geist and his co-workers,<sup>64</sup> Hamblen<sup>65</sup> and others agree that it is useless for this purpose in the clinic. Hartman<sup>67</sup> likewise found it to yield "far from promising" results when tested on the laboratory primate, the macaque monkey.

**Pituitary extract** Trials were also made with extracts of the anterior lobe of the pituitary gland of sheep. Zondek and Aschheim<sup>68</sup> and Smith and Engle<sup>69</sup> originally demonstrated the dependence of follicular maturation on the anterior hypophysis. Pincus<sup>70</sup> marshals much laboratory data on

the rabbit to show that this gland materially influences the ripening of ovum and follicle. Unreported trials with a commercial preparation of this material in my clinic failed utterly to accomplish anything among a group of anovulatory patients. Research is now in progress with an improved extract from sheep's anterior hypophysis, which is giving encouraging results, but only in follicular growth and in the production of uterine bleeding.

**Serum gonadotrope** Recently, there came to hand the potent follicle stimulating hormone from the serum of pregnant mares. Davis and Koff,<sup>71</sup> Siegler and Fein<sup>72</sup> and Hall<sup>73</sup> had reported great success with it. Although we<sup>74</sup> tried many different dosages and sequences in 48 patients, our results convinced us that this hormone, too, was quite unsatisfactory as a maturing hormone for human follicles. The recent report of Geist and his associates<sup>69</sup> substantiates our findings.

**Chorion hormone and serum gonadotrope** Hissaw, Greep and Fevold<sup>75</sup> showed that a critical proportion of follicle stimulating and luteinizing hormones made juvenile female monkeys ovulate. Since the chorion hormone is predominantly luteinizing, and the serum gonadotrope is in laboratory animals almost always only follicle stimulating, it was hoped that a combination of the two in sequence or combined in various proportions would produce the desired result. Among 22 anovulatory patients given these hormones in different doses, combinations and sequences, not one gave evidence of ovulation.<sup>74</sup> Hamblen<sup>68</sup> reports greater success with such combined and cyclic forms of therapy. I still believe, on the basis of laboratory studies on animals, that a particular combination and sequence of chorion hormone and serum gonadotrope may prove satisfactory. A better way would be to regulate the patient's own glandular system, if one only knew how.

**Estrogen** Zondek<sup>76</sup> and others have shown in animals that small doses of estrogen are stimulating to the anterior hypophysis, which responds by increasing its maturation influence on the follicle. Greep's<sup>77</sup> preservation of the corpora lutea of pregnancy, by injection of estrogen in rabbits from which both the hypophysis and the uterus had been removed, suggests that the mediation of the hypophysis is not always necessary.

Similarly, in human beings, repeated small doses of estrogen occasionally seem to exert a stimulating effect on the ovaries. Larger doses inhibit the pituitary gland, and if given daily for three or four weeks, commonly prevent ovulation in the regularly ovulating woman. Estrogen, then, is a

means not to be depended on, but one that apparently causes no permanent damage and in small doses may occasionally support follicular growth. Better results from pituitary gonadotrope may be obtained if small doses of estrogen are given simultaneously. The dosage must be nicely adjusted to the individual patient, for surely estrogen inhibits follicular growth if given in large quantities.<sup>78</sup>

### X-Ray

In 1935, Mazer and Spitz,<sup>79</sup> in a report of their own work, gave utterance to the scattered experiences of many other clinicians by stating that so-called "stimulating doses" of x-ray would bring about ovulation in approximately 50 per cent of patients with amenorrhea, and would regulate (possibly by establishing ovulation) the menstrual flow of women suffering from aperiodomenorrhea—dysfunctional uterine bleeding. These results were confirmed in a later series of cases by Mazer and Baer.<sup>80</sup> Rutherford<sup>81</sup> analyzed the cases treated in my clinic, and likewise showed that ovulation occurred in about 54 per cent of the anovulatory patients whose ovaries were exposed to 50 or 60 r three or four times at weekly intervals. This treatment, I believe, should be kept as a last resort. The x-ray is not stimulating; it is destructive. It causes atresia of follicles from the more advanced to the youngest, according to the degree of exposure. The subsequent ovulation in the favorable cases is commonly attributed to the removal of a follicular influence that inhibited the pituitary gland. In some of the unfavorable cases, it may merely fail to do this, but it possibly also has a deteriorating effect on the growth impulse of the germinal epithelium, which thereafter may fail to produce any new oocytes, or to produce normal ones that can mature. From the uniform results of geneticists,<sup>82, 83</sup> one may be sure that even though ovulation is effected, the genes of the entire germinal epithelium thus exposed are changed; and one may well fear for the results in progeny when two germ cells, both descended from irradiated epithelium, are combined in the third or fourth generation. This may not seem an imminent consideration, but I now believe it should be one, and that x-ray treatment, although an attractive escape from a therapeutic morass, should therefore be avoided if possible.

\* \* \*

It will be seen from the foregoing that I consider the hormonal treatment of anovulation to be definitely in a barely encouraging experimental stage. The first attack should be by copious use

of hygienic and dietary measures, supplemented by small doses of thyroid and very small doses of estrogen. An improved pituitary extract may be forthcoming. If available, this should be added to the other measures, alone or in conjunction with chorion hormone, in nicely timed injections. X-ray therapy should serve as a last resource. My observation of the stubborn anovulators, especially of the amenorrheic type, leads me to believe that more careful attention to diet and hygiene during the pediatric years might prevent much gynecologic difficulty. Studies directed to the frequency of ovarian dysfunction in antecedents and relatives of patients exhibiting this derangement might also prove helpful, by establishing an inheritable factor.<sup>84</sup>

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 27491

#### PRESENTATION OF CASE

A sixty-three-year-old locomotive engineer was admitted to the hospital because of painful and difficult urination, and aching and swelling in the right forearm.

Two years before entry, the patient began to have nocturia. After a year, the stream became small and difficult to start, and urination was quite painful. A local physician catheterized the patient periodically thereafter, and told him that he had "chronic inflammation" of the urethra and an "enlarged" prostate. Four months before entry, he began to have a steady ache in the right wrist. He noticed that when he was at work in his locomotive the ache was worse when he rested his right forearm "flat" than when he rested it on its ulnar surface. Two weeks before entry, the right wrist began to swell.

The patient's mother had died of "cancer of the liver." As a youth, he had a "soft chancre" and a bubo in his groin. About forty years before entry, he suffered a severe burn of his right leg. On two subsequent occasions, he fractured this leg. He dislocated his left wrist once and his right wrist twice, the last accident occurring ten years before entry. He had always had a very dry, easily chapped skin. He had had a chronic morning cough, with small amounts of sputum, for fifteen years before entry.

He had been seen in the hospital fourteen years prior to the present admission, because of tremor, dyspnea and palpitation of a year's duration. The thyroid gland was enlarged and firm. The basal metabolic rate was + 40 per cent. Auricular fibrillation was present, and responded to quinidine therapy. A subtotal thyroidectomy was performed (pathological diagnosis: hyperplasia), and the patient discharged improved.

On the present admission, examination showed an obese, apparently healthy man, with unremarkable heart, lungs and abdomen. The prostate gland was very small and of fibrous consistence, without palpable nodules. There was a firm swelling in the region of the head of the right radius, with redness of the overlying skin and local heat. The skin, as a whole, was dry and scaly.

The temperature, pulse and respirations were normal; the blood pressure was 140 systolic, 85 diastolic.

Examination of the blood showed a white-cell count of 9400 with 67 per cent polymorphonuclears, and a red-cell count of 4,280,000 with 13 gm. hemoglobin. The blood Hinton reaction was negative. The blood calcium was 9.3 mg., and the phosphorus 3.1 mg. per 100 cc.; the phosphatase was 3.5 Bodansky units. The nonprotein nitrogen was 12 mg. per 100 cc., and the urine showed a + test for albumin.

A roentgenogram of the right wrist showed a number of areas of destruction in the distal extremity of the radius, with some periosteal formation of new bone on the margins of the adjoining part of the shaft. Very little atrophy was present. Both medulla and cortex were involved, and there was definite soft-tissue swelling posterior to the involved joint. Roentgenograms of the pelvis and the chest were negative.

On the ninth hospital day, an operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR. GRANTLEY W. TAYLOR: This is a confusing story, and I think we are not going to get far with it until we see the x-ray films. Then it is going to be a matter of guessing the diagnosis. May we see the x-ray films first?

DR. JAMES R. LINGLEY: This is the area of destruction, rather a lobular area, in the lower extremity of the radius. In the lateral view, one can see destruction of the cortex posteriorly and definite thickening and edema of the soft tissues.

DR. TAYLOR: Somewhere in this interpretation, it speaks of the involved joint. That is just a loose method of expression, I take it. You do not see anything in the films to show that there is an involved joint?

DR. LINGLEY: No.

DR. TAYLOR: On reading the history, I became progressively more confused and gave thought to a number of things that I might have to consider when I saw the pictures. The patient dislocated his wrists some time before admission. I do not know what happened, but such dislocations are extraordinarily rare. I wondered if he had old traumatic arthritis, with absorption and new-bone formation around the joint, especially because of the allusion to the joint in the interpretation. Very much against that diagnosis are the facts that no atrophy was observed by x-ray study, and that motions were carried out with apparently adequate range. Then, I considered the question whether he had punched-out areas

in the bone near the joint, due to gout. There was nothing in the history either for or against it. The question of infection arose very strongly in my mind, because of the urologic difficulties—chronic urethral discharge, painful urination and a history of a soft chancre and bubo; it seemed to me that we might reasonably consider the possibility of gonorrheal arthritis in this case.

Syphilis of the bone, Charcot joint or gumma, it seems to me, reasonably enters into the possible diagnosis. However, the negative blood Hinton reaction, the fact that this lesion was painful and the fact that it was not in a weight-bearing joint all argue against anything like a Charcot lesion.

Tuberculosis of the bone is very unusual at this age, but it may occur, especially in the vicinity of a joint. Pyogenic osteomyelitis is also a very reasonable possibility. Against it are the normal chart, the normal white-cell count and the lack of a preponderance of polymorphonuclears in the differential count.

Then we move on to the consideration of neoplastic diseases of the bone. The patient was in an age group in which such diseases as Ewing's tumor and osteogenic sarcoma are rare. The latter occurs in this age group almost exclusively in association with very extensive Paget's disease of the bone, of which we have no evidence. The reticulum-cell-sarcoma type of lymphoma, which has recently been established as a clinical entity, is a rather capricious disease in the sense that we have not seen enough cases to say what its usual habits are, or what clearly defined characteristics it has on clinical observation or x-ray examination. It is something that must be considered and is hard to rule out. Hodgkin's disease of the bone, almost invariably associated with Hodgkin's disease elsewhere, also gives a confusing x-ray appearance and is sometimes very difficult to identify. A single plasma-cell myeloma should definitely be considered. I believe it is very unusual in a location of this sort. No mention is made of the serum protein or the possibility of Bence-Jones protein in the urine, or any of the other characteristics on which that diagnosis could reasonably be based.

Finally, we come to metastatic neoplasms. Metastases are very unusual below the elbows and knees, but they may occur. If we consider the diagnosis of metastases, we must find a primary focus of disease. We have no evidence of a primary focus anywhere. The concomitant problem this patient presents is urinary-tract difficulty. The small prostate, one that is not nodular, does not suggest a neoplasm. The negative spine and pelvis

plates practically rule out the possibility of metastases.

To all these possibilities, there are good objections, but it seems to me that we must at least have "got warm" somewhere in this rehearsal of the list of diseases. I should think that the objections to pyogenic osteomyelitis are less convincing than those for most of the other conditions. We have seen a number of cases of pyogenic osteomyelitis in which there was no elevation of temperature and in which there was no particular change in the leukocyte count, which is unusual. Let us consider that diagnosis in the light of the x-ray findings. We have surprisingly little new-bone formation. It is described in the notes, but is not a conspicuous feature in the study of these x-ray films. We do have rarefaction in the bone, but without surrounding condensation of bone, which is commonly seen around the Brodie's abscess type of chronic, indolent bone infection. In favor of pyogenic osteomyelitis are soft-tissue swelling, which is not definitely a tumor, and edema of the tissues, which is less commonly found in conjunction with neoplasm than with inflammatory conditions. It seems to me that pyogenic osteomyelitis is the most probable diagnosis. I should definitely entertain, in the background, however, the possibility of primary malignant neoplasm.

Dr. Lingley can probably contribute to this discussion by further comment on the x-ray films, considering the diagnostic problem that they present; the diagnosis in this case is almost entirely a problem for the roentgenologist and pathologist.

DR. LINGLEY: As Dr. Taylor has remarked, the presence of edema of the soft tissues is an important finding in ruling out a tumor in this case. We very rarely see either a malignant or a benign tumor with such definite edema as we have in this case. I think that the presence of edema immediately puts the lesion in the infection group. The question now comes up whether it is pyogenic infection, syphilis or tuberculosis. I think the roentgenologic appearance fits very beautifully a pyogenic infection. There is destruction, with some periosteal new-bone formation. Tuberculosis is almost always entirely destructive. There can be new-bone formation in tuberculosis, but in this case there is more than one would expect if it were tuberculous. Syphilis is a definite possibility. The type of periosteal reaction in this case could be classed as the lacelike type of periosteal bone formation that one sees in syphilis. I should place pyogenic osteomyelitis as the first diagnosis, and syphilis as the second.

DR. ALLEN G. BRAILEY: Is the fact that the phosphatase level was normal of any help?

DR. TAYLOR: I should think not. Dr. Franseen has studied these reactions. A high phosphatase level is evidence of osteoblastic activity. We may see a very high one in diseases like Paget's disease, and with some of the osteogenic sarcomas. On the other hand, it may be fairly low in cases of bone sarcoma, especially when there is not a great deal of osteoblastic activity. The low figure in this case might be taken as evidence against osteogenic sarcoma, but I do not believe that it would be indisputable evidence. Some of our osteomyelitis cases have had high phosphatase levels.

DR. CLIFFORD C. FRANSEEN: I agree entirely. The normal phosphatase and the absence of evidence of new-bone formation fit together. That is all one can say.

#### CLINICAL DIAGNOSIS

Osteomyelitis?  
Lymphoma?

#### DR. TAYLOR'S DIAGNOSIS

Pyogenic osteomyelitis.

#### ANATOMICAL DIAGNOSIS

Chronic osteomyelitis of radius (*Staphylococcus aureus*).

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This patient was operated on, and when the cortex was incised a free flow of pus was obtained. The material curetted from the cavity showed chronic inflammation and no evidence of neoplasm. Cultures of the pus showed *Staphylococcus aureus*.

A PHYSICIAN: What about the urinary tract?

DR. MALLORY: I know nothing more about that. The patient is still convalescing.

#### CASE 27492

#### PRESENTATION OF CASE

A seventeen-year-old Portuguese-American student was admitted to the hospital because of swelling of the left leg.

The patient was well until about six months before entry, when he noticed painful swelling of his right shin. He thought that he had struck the shin against hard objects on several occasions. The swelling gradually increased. After a few months, a local physician was consulted. After a roentgenogram of the leg was taken, a biopsy was requested and refused. Several months later, the patient came to the hospital.

On admission, the patient appeared healthy; the heart, lungs and abdomen were normal. There was a diffuse, bony hard, fusiform swelling on the posteromedial aspect of the left tibia, involving the middle third of the shaft, continuous with the normal portions of the shaft at its margins.

The temperature, pulse and respirations were normal; the blood pressure was 120 systolic, 70 diastolic.

Examination of the blood showed a white-cell count of 13,200 with 74 per cent polymorphonuclears, and a red-cell count of 5,070,000 with 85 per cent hemoglobin. The blood calcium was 11.6 mg. and the phosphorus 3.8 mg. per 100 cc., and the phosphatase was 6.3 Bodansky units. The blood Hinton reaction was negative. The urine was normal. A tuberculin test was negative in a 1:10,000 dilution.

A roentgenogram of the left leg showed a fusiform thickening of the tibia, at the junction of the upper and middle thirds. The periosteum in this area was markedly thickened, and in one or two places there was slight roughening of the periosteum, with some destruction. There was very slight soft-tissue thickening, superimposed. A cavity, measuring 1 by 1.5 cm., situated at the base of the region of periosteal formation of new bone, was visible only on a film that had been much overexposed.

On the seventh hospital day, an operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR. THOMAS ANGLEM: May we see the x-ray films?

DR. JAMES R. LINGLEY: Here we see the area of fusiform thickening described, which is due mainly to the gross thickening of the cortex on the posterior margin of the shaft. In the overexposed film, there is one small linear area of rarefaction about 1.5 cm. in length within the area of new-bone formation, but I cannot demonstrate it with this light. There is no surrounding soft-tissue mass, and no edema of the soft tissues.

DR. ANGLEM: There is very little in this story that is of any diagnostic aid. It seems to me, as in the last case, that the diagnosis rests on the interpretation of the x-ray films. The essential finding in the history is a story of progressive swelling of the tibia for six months, associated with some pain. At the time of examination, the boy was apparently still in good general health, with normal temperature, moderate leukocytosis—13,200—and a slight elevation in the serum-phosphatase level; otherwise, the findings were essentially negative. We get some assistance from



consideration of certain negative findings. The tuberculin test was negative in a 1:10,000 dilution. This, coupled with the x-ray picture, which has none of the usual characteristics of a tuberculous bone lesion, I think, permits us to rule out tuberculosis. The blood Hinton reaction was negative; however, this lesion conceivably could be syphilitic on the basis of its x-ray appearance. It shows a degree of condensation in the cortical bone consistent, I think, with syphilitic osteitis, and the area of destruction might also be explainable on the basis of a syphilitic lesion. However, it would be very hazardous to make a diagnosis of bone syphilis in the presence of a negative blood Hinton reaction. I believe that we can disregard syphilis as a possibility.

The diagnosis comes down to a choice between a low-grade infectious process of bone and malignant tumor. Of the malignant tumors, I think only two need be considered seriously—endothelioma of bone and osteogenic sarcoma. The position of this lesion is typical of what we usually see in Ewing's sarcoma, but the other features of the disease are lacking. It is unusual to see this degree of sclerosis or condensation of bone in Ewing's tumor, and the sharply localized small area of destruction is not the usual picture. We can rule out Ewing's sarcoma.

Osteogenic sarcoma usually occurs in the metaphysis and is relatively uncommon in the mid-shaft of the bone. Nevertheless I think that it must be considered a possibility. On the whole, this picture does not seem to me to be the picture of osteogenic sarcoma. The usual classic features of the disease are lacking. There is no reactive triangle that I can make out. The small area of destruction seems to be sharply localized, and the area of reactive bone is much more diffuse and spreads around the entire circumference of the bone rather than being limited to the area in which the destruction is apparent.

A low-grade infection of the bone seems the most likely possibility here. As in osteogenic sarcoma, it also occurs most commonly in the metaphysis rather than in the shaft, but in contrast with the usual form of acute hematogenous osteomyelitis, which occurs predominantly in the very young, the subacute and chronic forms occur very frequently in the shaft and are relatively common in older children and young adults, the age group in which this patient falls. The absence of any definite soft-tissue swelling and the absence of tumor are against infection. Nevertheless, in any extremely low-grade process existing for a long time, it is possible to have infection without any superimposed soft-tissue swelling or edema. The

sharply localized punched-out area in the cortex seems to me to suggest, from the x-ray appearance, a cortical abscess more than an area of destruction from a malignant tumor, and the periosteal reaction in the surrounding bone is consistent with a low-grade infectious process. I should say that the first and most likely possibility in this case is low-grade infection, —osteomyelitis,—with osteogenic sarcoma as a definite possibility.

DR. TRACY B. MALLORY: Dr. Lingley, do you want to discuss the radiologic aspects further?

DR. LINGLEY: I agree with Dr. Anglem in his diagnosis. I think the picture is very characteristic of Garré's<sup>1</sup> sclerosing osteomyelitis. It is a low-grade infection that has been present for a long time, producing dense, well-organized new bone. The character of the new bone is very much against any type of tumor. Ewing's sarcoma is the most likely tumor in a location involving a large area of the shaft, but there is no onion-peel formation and not enough destruction, and the new bone is too dense and well organized.

DR. GRANTLEY W. TAYLOR: In one x-ray film, there is a suggestion that there has been distortion of the weight-bearing line of the tibia. If that is a correct interpretation, it seems to me that it is a finding we have observed in a number of cases of osteomyelitis in the shaft of the bone: definite overgrowth on one side, with a slight distortion of the axis of the bone.

#### CLINICAL DIAGNOSIS

Osteoid osteoma.

DR. ANGLEM'S DIAGNOSIS

Low-grade osteomyelitis.

#### ANATOMICAL DIAGNOSIS

Osteoid osteoma of tibia.

#### PATHOLOGICAL DISCUSSION

DR. MALLORY: Shortly after admission, the patient was seen in the Tumor Clinic, where the consensus was that this was an inflammatory lesion, because of the comparative lack of symptoms, and that biopsy was not indicated. It was suggested that the x-ray films be reviewed again. The patient was later seen at the surgical grand rounds, where, in contrast, biopsy was advised. Eventually it was done. A considerable section of the cortex was removed, cutting down to and including the minute area of rarefaction, which Dr. Lingley believed was there but could not satisfactorily demonstrate in this light. The histologic section has a line of dark red across it, 1.0 cm. in length and 0.4 cm. in width, which corresponds

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## INSTRUCTION IN FIRST AID CARE

AN article appearing elsewhere in this issue of the *Journal* calls attention to the importance of instructing laymen in first aid care, not only because of the value of such knowledge in handling the possible civilian casualties of war but also because of its usefulness in giving proper immediate care to the millions of people who are injured each year in automobile and industrial accidents.

Various courses have been sponsored by the American Red Cross, and although over three million certificates have been issued since 1910, it is only within the last two years that the population as a whole, stimulated by the national emergency, has become properly appreciative of what it can contribute if adequately trained in first aid care. Interest has been largely promoted by the

training of thousands of instructors by the American Red Cross, who, in turn, have conducted the classes for civilian defense workers, employees of industrial plants and business establishments, service men and those employed by various local and state governmental bureaus.

Many physicians, unfortunately, seem to have been rather indifferent to this effort—some because of a belief that first aid care cannot be properly given by a layman and others because they are ignorant of what such care comprises. There is no doubt, however, that many of the procedures with which the trained layman is familiar may result in the saving of life or the prevention of severe and permanent crippling, and all physicians should familiarize themselves with the methods of first aid care and should, if possible, register with their local Red Cross chapters as instructors in standard or advanced first aid courses.

A booklet, *Advanced First Aid for Civilian Defense*, has recently been prepared by the American Red Cross in collaboration with the Medical Division of the Office of Civilian Defense. This ten hour course is intended for the personnel of emergency medical field units, for air raid wardens and for members of other civilian-defense groups. Although alone inadequate for nonmedical workers, it furnishes minimum instruction when supplemented by repeated drilling under competent supervision. Physicians who are members of emergency medical field units should conduct the instruction and obviously should be thoroughly acquainted with the contents of the booklet, copies of which can be obtained from the First Civilian Defense Region, 101 Milk Street, Boston.

## CHRISTMAS SEAL CAMPAIGN AND NATIONAL DEFENSE

BECAUSE of the national emergency, the forthcoming Christmas Seal Campaign of the National Tuberculosis Association merits even greater attention and more generous support than the campaigns of other years. Each week brings the European conflict closer. The recent sinkings of American ships in the waters of the Western Hemisphere emphasize the need for more than

vague and half-hearted — and therefore fumbling — program of defense. A united and determined nation, willing to sacrifice temporary comforts and luxuries, must be ready to meet a very real threat. The question of *when* defense is to be achieved now holds little more than academic interest; the question of *how* is all-important.

The crux of the defense effort is good health: a healthy and expertly trained army and navy can be equipped only with the arms produced by industrial workers, who must be protected from sickness; a healthy general population must encourage and support the military and the industrial army — the morale of the whole nation could easily be weakened by widespread disease. Thus, tuberculosis, which still ranks seventh as a cause of death in America and is still the chief killer in the age group that is most vital for national defense, must be eliminated not only from the armed forces and workers in industry, but also from the ranks of those who must endure the restrictions, privations and dislocations of a war-time economy.

The death rate from tuberculosis has been cut 75 per cent since the first sale of Christmas Seals, in 1907. But until the disease has become a curiosity of medical history, — that is, until the death rate has been cut 100 per cent, — there must be no lag in the fight against it; medical knowledge is at present sufficient to stamp it out, but a vast expenditure of money and energy must be available before that goal can be attained. Organizations like the National Tuberculosis Association can function only with the support of the public and the medical profession.

The Christmas Seal Campaign this year presents a double challenge to patriotic and humanitarian impulses: by contributing generously, laymen and physicians can help free the armed forces and the civilian population of tuberculosis, and at the same time they can achieve progress toward the goal of complete eradication, so that in the days of peace a healthy nation can enjoy the liberty, happiness and prosperity it must now fight to preserve.

## MEDICAL EPONYM

### LEGG-CALVÉ-PERTHES'S DISEASE

This condition was first described as an entity by Arthur T. Legg (1874-1939) when he was junior assistant surgeon at the Children's Hospital, Boston, in a paper read at the annual meeting of the American Orthopedic Association in June, 1909. The paper was published under the title, "An Obscure Affection of the Hip-Joint," in the *Boston Medical and Surgical Journal* (162: 202-204, 1910). The author reported five cases, with x-ray photographs, and said:

. . . the following facts . . . are observed:

- (1) Age, five to eight years.
- (2) History of injury.
- (3) Limp.
- (4) Thickening about the neck of the femur.
- (5) Absence of pain.
- (6) Absence of constitutional symptoms.
- (7) Little or no spasm.
- (8) Absence of shortening. . . .

We have considered a group of cases all presenting practically the same conditions . . . which are to my mind atypical of any condition heretofore described. . . . I make no claim to any definite conclusion.

Jacques Calvé, while assistant surgeon of the marine hospital at Berck, wrote a paper, entitled "Sur une forme particulière de pseudo-coxalgie greffée sur des déformations caractéristiques de l'extrémité supérieure du fémur [A Special Form of Pseudotuberculosis of the Hip, with Characteristic Deformities of the Upper Extremity of the Femur]," which appeared in the *Revue de Chirurgie* (42: 54-84, 1910). A portion of the translation follows:

In the past three years, I have had the opportunity of seeing 10 cases of chronic arthritis of the hip that ran a distinctly typical course and were clearly defined both clinically and radiographically, not corresponding to any type previously described and at first considered to be coxalgia, from which they differed in several respects.

As may be seen on reading the notes that we have given at the end of this article and from the examination of the radiographic pictures that accompany them, the chief characteristics of these arthritides are:

- (1) Signs of a reaction about the joint, running a chronic or subacute course and healing without any limitation of motion.
- (2) Bony deformities preceding these articular symptoms and persisting after their disappearance. These are:
  - (a) Coxa vara.
  - (b) Hypertrophy of the head of the femur.
  - (c) Atrophy and lamellar deformity of the center of ossification of the head.
  - (d) Complete absence of bony destruction. . . .

These arthritides occur in young subjects between the ages of three and one-half and ten years

In 1913, Professor Georg Perthes (1869-1927), director of the surgical clinic at Tübingen, delivered an address, 'Ueber Osteochondritis deformans juvenilis [On Osteochondritis Deformans in Young Persons]', which was published in the *Archiv für klinische Chirurgie* (101: 779-807, 1913). He stated that several observers had reported cases of this condition, mentioning his own observation in the *Deutsche Zeitschrift für Chirurgie* (107: 111-159, 1910), under the title *Ueber Arthritis deformans juvenilis [Concerning Arthritis Deformans in Young People]*, but apparently was unfamiliar with Legg's description. He stressed the value of recognizing the nontuberculous nature of the condition. A portion of the translation follows

In this disease, which I should like to discuss here as osteochondritis deformans of the hip in young persons, we are dealing with a peculiar wasting away of the upper epiphysis of the femur, which originates in a subchondral focus of destruction and is complete only after a course of some years. After careful studies, and as the result of work done in company with my assistant, Dr Schwarz, I have arrived at the opinion that in these cases we are dealing with a disease process fundamentally different from the arthritis deformans of adults, and also that the other conception which exists in regard to this condition, namely that it is a tuberculous affection of the upper femoral epiphysis, is not justified. We are rather dealing with a peculiar, unique process, which regularly leads to a characteristic clinical picture and apparently is self limited.

A careful and detailed description of the condition follows, with case histories and x-ray pictures

R W B

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

#### FATAL NAUSEA AND VOMITING IN PREGNANCY

A twenty four year-old primipara entered the hospital at the end of the third month, with a diagnosis of nausea and vomiting of pregnancy.

The history states that the patient had been vomiting practically everything for the four weeks be-

fore admission, her weight was 90 pounds, which represented a loss of about 40 pounds. On physical examination, the pulse was 140. There was some tenderness over the region of the liver. An icteric index determination and liver function test showed evidence of liver damage. The patient was given 10 per cent glucose solution intravenously, and four days later it was decided that abortion should be induced. The cervix was dilated, a catheter inserted, and the vagina packed with gauze, in addition to 5 minim doses of pituitary extract every fifteen minutes for ten doses.

On the following day, the catheter and gauze pack were removed, and the fetus was passed spontaneously. Subsequently, the patient did not improve and, in spite of stimulation, died four days later. No autopsy was performed.

*Comment* This case is evidence that, when poorly treated, the nausea and vomiting of pregnancy may still become pernicious and even result in death. Since this patient had had no medical care until she entered the hospital, her death is due solely to neglect on her own part.

Such patients die solely of starvation. Had the patient consulted a physician when the first distressing symptoms of nausea and vomiting appeared and had simple home remedies proved of no value, hospitalization should have been advised. The treatment then would have been rest in bed, sedation, intravenous glucose (2000 cc a day), thiamin chloride intramuscularly in large doses and no food by mouth for several days. Small feedings through a Levine tube might have been necessary, but most patients whose condition does not become too serious recover without tube feeding.

The loss of weight from 130 to 90 pounds shows how poor this patient's general condition was when she arrived in the hospital. The pulse of 140 was another indication of the seriousness of her condition. Abortion, which was the only possible recourse, proved unavailing. Such deaths, when patients are intelligent and consult medical advice, are absolutely unnecessary.

If the statement in the record that, after the catheter had been introduced and the vagina packed, 5 minim doses of pituitary extract were given every fifteen minutes for ten doses is correct, one can only be amazed. Small doses of the drug to stimulate labor after this method of abortion has been attempted may possibly do some good, but large doses are not only contraindicated but might cause harm. Ordinarily, there is no need of using pituitary extract when abortion is done in this manner.

\*A series of selected case histories by members of the section will be published weekly. Come in and question by subscription are solicited and will be discussed by members of the section. Letters should be directed to Dr. Raymond S. T. U.S. Secretary, 330 Dartmouth Street, Boston.

## DEATHS

**BLACKFAN**—KENNETH D. BLACKFAN, M.D., of Boston, died November 29. He was in his fifty-ninth year.

Born in Cambridge, New York, Dr. Blackfan received his degree from Albany Medical College in 1905. He was pathologist and bacteriologist at the Albany Hospital from 1905 to 1907, instructor in pediatrics at the Polyclinic Hospital, Philadelphia, in 1910 and 1911, and assistant at Washington University School of Medicine, St. Louis, in 1911 and 1912. From 1912 to 1918, he taught at Johns Hopkins University School of Medicine, where he was associate professor of pediatrics from 1918 to 1920. He was professor of pediatrics at the University of Cincinnati College of Medicine from 1920 to 1923, and from that time until his death was professor of pediatrics at Harvard Medical School. He was chief of the medical staff at the Children's Hospital, and was associated with the Infants' Hospital. He was a member of the American Academy of Pediatrics, director of the American Child Health Association, and a fellow of the Massachusetts Medical Society and the American Medical Association.

He is survived by his widow and a son.

**LYON**—FREDERICK D. LYON, M.D., of Cambridge, died November 27. He was in his seventy-third year.

Dr. Lyon received his degree from Harvard Medical School in 1896. He was a former member of the Massachusetts Medical Society.

## DEFENSE ACTIVITIES

## UNITED STATES ARMY

The following medical officers entered on active duty between November 15 and 22, 1941:

**BEGG, CHARLES F.**, 1st Lieut., of Providence, Rhode Island; Station Hospital, Camp Edwards, Massachusetts.

**DEL CAMPO, DANTE**, 1st Lieut., of Lynn, Massachusetts; Westover Field, Massachusetts.

**GLENDY, ROBERT E.**, Capt., of Newton, Massachusetts; Station Hospital, Fort Banks, Massachusetts.

**JADOSZ, FRANK C. J.**, 1st Lieut., of Providence, Rhode Island; Army Air Base, Bangor, Maine.

**MORRISON, JONATHAN I.**, 1st Lieut., of Waban, Massachusetts; Westover Field, Massachusetts.

**STARBUCK, GEORGE W.**, 1st Lieut., of Boston; Station Hospital, Camp Edwards, Massachusetts.

**WALKER, DONALD A.**, 1st Lieut., of Worcester, Massachusetts; Army Air Base, Bangor, Maine.

## CIVILIAN DEFENSE

## X-RAY FACILITIES

The Medical Division of the Massachusetts Committee on Public Safety requests that all who operate private x-ray laboratories register with the committee the types of machines they operate, including the current necessary, with additional advice whether, in the event of a national emergency, they would be willing to have their machines moved to hospitals for public use. This information will, of course, be kept confidential, and no action will be taken without consultation with the owners. Communications should be addressed to Dr. Elliott C. Cutler, medical director, Massachusetts Committee on Public Safety, 18 Tremont Street, Boston.

## RADIUM

In England, when an alert is sounded, all who possess radium are required to lower it into a well or pit about 50 feet deep, to do away with the danger that would occur should radium be scattered about in public places. All who possess radium should take some precaution for its proper disposition in the event of bombing.

## REGIONAL MEDICAL OFFICER

Mayor F. H. LaGuardia, director of the Office of Civilian Defense, Washington, D. C., recently announced that Dr. Allan M. Butler, of Boston, had been commissioned senior surgeon in the Reserve of the United States Public Health Service and had been called to active duty as regional medical officer in the First Civilian Defense Region, with headquarters in Boston. The area of jurisdiction corresponds with that of the First Corps Area of the United States Army.

## MISCELLANY

## AMERICAN MEDICAL ASSOCIATION BROADCASTS

"Doctors at Work," the dramatized radio program broadcast by the American Medical Association and the National Broadcasting Company, will go on the air for its second season on Saturday, December 6, from 5:30 to 6:00 p.m., E. S. T. The program is broadcast widely from the more than seventy-five stations affiliated with the Red Network of the National Broadcasting Company and is heard from coast to coast.

Last year, the broadcast was a serialized story dealing with the experiences of a fictitious but typical American boy choosing medicine for his vocation and proceeding to acquire the necessary education and hospital training for the private practice of medicine. Interwoven with the personal story of young Dr. Tom Riggs and his fiancée, Alice Adams, was the romance of modern medicine and how it benefits the physician's patients.

The new series of broadcasts will resume where last year's story left off, namely, with the marriage of Tom Riggs and Alice Adams, and the subsequent life of a young physician and his wife at the time of a national emergency in a typical, medium-sized, American city.

## NOTE

Dr. Russell F. Sullivan has been appointed professor of orthopedic surgery at Tufts College Medical School. He is at present visiting surgeon at the Boston City Hospital.

## CORRESPONDENCE

## ELIGIBILITY FOR SUBSCRIPTION TO MEDICAL-SERVICE PLANS

*To the Editor:* Differences of opinion exist among both laymen and physicians regarding the financial groups to which a prepayment medical-service plan should be available. In a discussion of this subject, the difference between voluntary and compulsory medical-service plans should be kept clearly in mind. This letter concerns itself only with voluntary plans.

Some believe that the Society's prepayment medical-service plan should apply only to the so-called "medically indigent," although it is generally conceded that it is difficult to define medically indigent because so many factors, such as size of the family and character of the ill-

ness, enter into the problem. Limitation of service to this group would mean that the subscribers would be made up chiefly from those who at the present time receive their medical care wholly or in part through institutions supported by taxation or private philanthropy. Students of these plans say that past experience shows that individuals in this group are unable and unwilling to pay such rates as are required to keep the plan from being a financial burden to physicians.

Others believe that service should be available to people in the income level above this charity group which roughly includes those on the borderline of charity up to those in the income level that offers a moderate degree of financial security. Many in this group are anxious not to be objects of charity but still need some method of establishing their financial security by being able to budget for health as well as other expenses. Throughout the country, the medical profession obtains a substantial amount of its income from this group at the present time. Some physicians fear that permitting such persons to become subscribers would make further inroads on their incomes, which have been invaded in recent years by the free clinics because patients have been forced to have recourse to such clinics as good medical care has become more and more expensive. It must be admitted that, if this group is permitted to become subscribers, those physicians who participate will find themselves caring for certain patients who formerly were on a fee for service basis. However, in answer to this, it may be said that, where there have been sufficient subscribers and proper economy in the management of the plan the funds from which physicians are paid have been sufficient to ensure a larger income for the same amount of work among this group than that on the fee for service basis. Furthermore, experience suggests that, under these medical service plans, subscribers obtain more medical service than they are willing to avail themselves of on the fee-for-service basis. It is reasonable to expect that, if the medical-care plan is successfully launched, certain patients from charity or tax supported clinics whose eligibility for such service is questionable will be returned to private practitioners. This will relieve the burden on moneys raised by taxation and the strain on private philanthropy.

Some laymen and physicians consider that prepayment medical service plans should be available to all the population at the same rates, just as hospital service plans are, or any other plans for budgeting the costs of services.

Experience shows that many persons object to subscribing to a medical service plan to which only those with certain incomes are eligible. Some of these objectors fear that this indicates cheap medicine others that it signifies class distinction and thus puts a stigma on them and still others that there must be something wrong with the plan if their superiors in industry are not eligible. With a consideration for these various apprehensions and disapprovals among laymen and physicians, can a simple program be developed regarding who should be eligible to subscribe and on what basis?

This program should guarantee equal service to all subscribers and ensure proper compensation for all participating physicians. It must also be attractive to potential subscribers, because experience has proved that the success of these plans depends on the number of voluntary subscribers, in fact, failure to secure a sufficient number of subscribers on a voluntary basis has been a strong argument for those who favor compulsory health insurance.

Still others believe that, if the plan is open to people of all income levels, there should be a sliding scale of

dues arranged in accordance with the subscribers' incomes. By careful adjustment of rates, it would probably not be necessary to eliminate as potential subscribers those in the higher income levels, because the rates in these levels would presumably be so high that few if any subscribers from this group would be interested. It has been suggested that under this arrangement a physician should receive more for the care of a subscriber who pays a higher rate than for the care of one who pays a lower rate. This seems fundamentally unsound because the amount of time and skill used by the physician toward any subscriber should be the same. The apparent injustice to the participating physician in not being able to obtain a substantial fee from the wealthy subscribers who formerly were patients on a fee for service basis might be equalized by the fact that the funds from which the doctors are paid would be substantially increased if any appreciable number of the subscribers came from the higher income levels, because of the higher rates such persons are charged. Thus, the physicians assured in care for work done under the plan might be appreciably better than on the fee-for-service basis and the physician would still have an opportunity to add to his income by caring on a fee for service basis for those in the higher income levels who would not wish to budget for their medical service.

Such questions as these deserve the careful consideration of physicians. A presentation and tolerant discussion of various aspects of these problems in the *Journal* should contribute much to their ultimate satisfactory solution.

CHANNING FROTHINGHAM, M.D.

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## REPORT OF MEETING

### ROBERT BRECK BRIGHAM HOSPITAL

At a meeting at the Robert Breck Brigham Hospital on October 27, Dr Carl C Seltzer delivered a paper entitled "Anthropometry and Arthritis. The difference between rheumatoid and degenerative joint disease." The report was based on several series of male and female patients who were at the Robert Breck Brigham Hospital either at the time of the study or at some other time. Despite the small numbers involved, the statistics were found to be scientifically significant. The various arthritides were accurately defined, and all cases were clinically assigned to one or the other group.

A study of the racial background revealed that the two groups were composed fundamentally of a cross-section of the surrounding population except for insignificant variations. Had this not been so, the entire study might well have been invalidated. Scrutiny of the age distribution revealed an average of fifty six years in the degenerative group as contrasted with thirty seven years in those with rheumatoid arthritis. Since age might be expected to play a role, a comparison was made between the 12 youngest of the former and 12 of the latter group who were found to be of the same age group.

It was determined that, although body weight may be expected to vary during the course of the disease, the rheumatoid patients were about 30 pounds lighter when measured either by best or admission weight, regardless of age. Similarly, those with rheumatoid arthritis were found to have a greater absolute and relative arm span. The upper body measurements revealed that the rheumatoid patients had narrower shoulders and chest cir-

cumference. Furthermore, the greater chest circumference of the patients with degenerative arthritis was not explained by the weight difference. The same tendency was borne out in a measurement of the intercostal angles, which were markedly narrower in the rheumatoid group.

Examination of the lower torso showed that the rheumatoid patients were also smaller in this region than the other group except in relation to chest circumference. The upper extremities in the former group were shorter in over-all measurement as well as narrower, with very long, narrow hands and a relatively long forearm. The most significant finding in the lower extremities was the relatively small distal femoral intercondylar measurement in the degenerative class.

As a result of these and further detailed statistical analyses of anthropometric measurements and proportions, it was concluded that the patients with rheumatoid arthritis were markedly different in bodily physique from those with degenerative joint disease. These differences persisted even after allowances were made for the age discrepancies between the two groups and the effect of the disease on various parts of the body. On the whole, it appeared that the patients with rheumatoid arthritis were distinctly more linear; they were narrower in the shoulders, chest and hips, and smaller in many muscular circumferences. There were certain anthropometric proportions in which the two groups were so markedly divergent that their frequency distribution showed only slight overlap. Another point of particular interest was the discovery of a strong tapering of the lower extremity among the group with degenerative joint disease. It was found that this type of patient had absolutely and relatively larger bodily dimensions above the hips for the size of the knee and ankle joints.

It was also pointed out that the group with rheumatoid arthritis could be subdivided into several types of body build in which the linear element was fairly strong. The group with degenerative joint disease, on the other hand, consisted mainly of a single type, which was characterized by strong laterality, stocky build and a large-boned, large-muscle and highly pyknic habitus.

The discussion was opened by Professor Earnest A. Hooton, of Harvard University, who stated that it was a statistical miracle that the differentials showed up so clearly with such small samples. He believed that larger groups would undoubtedly corroborate these data and bring out additional smaller but significant data. The suggestion was made that these characteristic body types probably mirror physiologic tendencies, and that an attempt should be made to discover certain physiologic proclivities of normal subjects of the same body types. In general, race is considered of importance only in ruling out the few racial characteristics that might interfere with an evaluation of the individual as such.

Dr. Walter Bauer, of the Massachusetts General Hospital, expected the study to reveal merely a cross-section of the general population and found the results disturbing. In his experience, 100 per cent of people in the sixth decade exhibit evidence of degenerative arthritis. It was stated that there is some difference of degree, the hospital population being the worse and therefore probably representing a selected group.

In closing, Dr. Seltzer stated that there is indeed a mixture of types, which is most marked in the rheumatoid patients, who actually represent the random sample. Dr. Bauer expected the degenerative group to be; the patients with degenerative disease are actually a very homogeneous group. Furthermore, an entirely independent

study in another section of the country gave substantially the same results.

## BOOK REVIEWS

*Lectures on Diseases of Children.* By Sir Robert Hutchison, Bart., M.D., LL.D., F.R.C.P., and Alan Moncrieff, M.D. Eighth edition. 8°, cloth, 471 pp., with 107 illustrations. Baltimore: Williams and Wilkins Company, 1940. \$6.75.

This is not a systematic treatise on pediatrics. It is a transcript of clinical lectures covering, for the most part, the commoner diseases of childhood and such other maladies as manifest themselves more differently in the child than in the adult. A knowledge of general medicine by the reader is assumed, and there is perhaps more emphasis on treatment and general management than on diagnosis.

Obviously, this book is intended to supplement, not to supplant, the usual textbooks. And it contains a good deal of sound, though, to the pediatric specialist, elementary, advice. Of course, in the matter of nonspecific treatments, there often are, even among the ablest of therapeutists, enough grounds for disagreement, and some measures, commonly acceptable, apparently, to our British brethren, are in less favor in this country. Moreover, some of the drugs called for are, at least under the names used in this book, unfamiliar to us. Local trade names, at any rate in a volume intended for foreign consumption, should never be used. It is also to be noted that some of the x-ray reproductions are on so small a scale as to be well-nigh worthless.

The value of this book in England is attested by the fact that it has reached this eighth edition. Unfortunately, it will probably be of less utility here.

*Accidental Injuries: The medico-legal aspects of workmen's compensation and public liability.* By Henry H. Kessler, M.D. Second edition, enlarged and thoroughly revised. 8°, cloth, 803 pp., with 202 illustrations. Philadelphia: Lea and Febiger, 1941. \$10.00.

With the advent of workmen's compensation laws, the medical and legal professions have been forced to develop a set of standards for appraising injuries. Kessler has summarized many of the isolated facts and experiences from the forty-eight states and has created a masterpiece of orderly thought on the numerous problems of accidental injuries.

In this book he gives a brief history of the progress in the field since Wisconsin passed the first state compensation law in 1911. There are many disparities in the present laws of the various states, but these will no doubt be erased as experience points the way to more workable and just legislation.

The introductory chapters are devoted to general considerations of workmen's compensation. There follows a section on specific injuries, which practitioners will find most helpful. Methods of examination, tests of function and evaluation of disability are considered for all types of injury and occupational disease. The facts and opinions collected here are encyclopedic in scope and can save much time in reaching a fair settlement. An extensive bibliography at the end of each chapter will be welcomed by those who wish more information on any specific subject.

(Continued on page x)



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## THE PRIVATE PHYSICIAN'S OPPORTUNITY IN INDUSTRIAL MEDICINE\*

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IN general, when one speaks of a private physician one means a physician who is primarily concerned with the protection of the health of individuals rather than of social groups. He is the physician who, in the course of his practice, is concerned with treating the physical ills, great or small, of patients who come to his office or whom he sees in the home, the clinic or the hospital. To offer his patients the benefits of the most up-to-date and the best medical knowledge, he wages a constant struggle to keep informed of the latest developments in medicine, a science that becomes more and more highly technical and specialized.

Because of the pressure of his practice and because he must keep abreast of technical advances, the private physician may lose sight of the fact that medicine has social and economic aspects, that he may forget that the social causes of illness are just as important as the physical ones, and that he lives and works in relation to a given economic and social system. He may be so absorbed in his work with individual patients that he fails to discern a larger problem—the opportunity and responsibility to serve society.

Yet, if the private physician is to act consciously and intelligently, he must have some knowledge of social and public health problems outside the immediate sphere of his routine practice—problems that he may consider, at first glance, to be completely unrelated to his work. One of these problems is that of industrial health.

All physicians are aware that the United States today is engaged in a program for the defense of its national interests. Furthermore, they know that the core of the defense program is industrial production—the speed with which adequate

quantities of vital defense materials can be supplied. How many physicians, however, are aware of the relation of a high level of industrial health to the attainment of a high level of industrial production? How many realize the nature and extent of the problem of industrial health, and the effect of industrial disability on production? How many recognize that they have an opportunity to help solve these problems and thereby not only to aid in the success of the national defense program, but also to make a contribution of great and lasting social value to the welfare of the Nation?

I shall briefly discuss the problems of industrial hygiene with which the private physician should be familiar, and the efforts that he can make toward their solution.

### *Nature and Extent of the Problem*

According to the latest census, the total labor force in the United States today is approximately 52,000,000—this gives some indication of the magnitude of the problem in terms of numbers alone. So far as the health status of this large group of workers is concerned, despite years of continued improvement in industrial hygiene, industrial accidents in the United States still take an annual toll of 18,000 lives and cause 90,000 permanent and 1,782,000 temporary disabilities. Many problems still arise from diseases peculiar to certain occupations, such as silicosis, lead poisoning and the dermatoses, most of which are preventable.

It is also well known that industrial workers have higher rates of physical defects than non-industrial workers, and that excessive mortality is especially notable in unskilled workers, among whom the death rate from all causes is 100 per cent or more in excess of the death rate among agricultural workers. Of greatest significance, however, is the enormous waste of life and efficiency resulting from nonindustrial illness among workers. As a matter of fact, the amount of

\*Presented before the New England Postgraduate Assembly, Cambridge, Massachusetts, October 29, 1941.

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time lost from work because of ordinary illness is fifteen times as great as the total time lost owing to accidents and occupational diseases combined.

### *Effect of Industrial Disability on Production*

The conditions cited as the cause of disability in industry account for an enormous loss in time—nearly 400,000,000 days a year. The monetary cost of this lost time runs into billions of dollars. In terms of defense materials, this lost time may be interpreted as the number of days it takes to build approximately 50 dreadnoughts of the *North Carolina* class, 165,000 combat tanks or 90,000 bombers. It is true that we know how to control the majority of industrial-health hazards, but it is also true that there is a lag in the application of that knowledge, just as there is a lag between knowledge and its application in other fields. If even a 10 per cent reduction in these time losses could be achieved, it is evident that much would have been done toward removing a serious obstacle to the success of the defense program and toward furthering the health of the Nation.

Needless to say, all these problems in industrial hygiene have become magnified with the present expansion of industrial activities. Preliminary data already indicate a marked rise in the incidence of accidents and occupational diseases among workers. Those who are concerned with maintaining the worker on the job at a high level of health and efficiency have a real responsibility. By creating safe and healthful working conditions *now*, the prospect of being faced in the future with thousands of men and women whose health has been irreparably damaged because of exposure to harmful conditions in industry will be minimized. This, to my mind, is the least we can contribute to the national defense effort.

I cannot presume to discuss mental hygiene, nutrition, the home environment of the worker, housing, and wages and hours, all of which are important aspects that should certainly be included in any serious discussion of the broader perspectives of industrial health.

### *Method of Attack*

Basically, the problems to be attacked can be divided into two types: those concerned with the hygiene of the individual, and those dealing with the environment in which the individual works. The first function comes within the scope of the medical sciences, and the second deals with engineering practices.

So far as the working environment is concerned, it is within the province of the medical profession to determine the existence of such diseases as may

be due to the working environment, whereas on the basis of the physician's findings, the engineer is in a position to learn what unhealthful conditions should be investigated and where control measures need to be initiated. It is essential therefore that the various professions clearly understand the functions of each and approach the solution of the industrial-hygiene problem as co-workers in a joint effort, co-operating with each other to the fullest extent.

Because nonindustrial diseases among industrial workers are just as common as and more serious economically than those among the general population, industrial hygiene has rightfully been considered a function of the general field of public health. It is for this reason that the medical profession plays such an important role, since it is one of the chief concerns of that profession to assist in the promotion of better health in the community.

### *Present Practices in Industrial Hygiene*

Industrial organizations are becoming more and more aware of their responsibilities concerning the protection and improvement of the health of employees. This is especially true of the large plant, which is in a better economic position to deal with this problem than the small plant, which finds it very expensive to provide more than a limited industrial-health service to its workers. Present-day trends indicate that industrial-hygiene services furnished by industry are on the increase and of late have been extended to include not only the prompt treatment of injuries and diseases arising from occupational exposures, but also other services, such as dental, ocular, x-ray and educational programs for health promotion. Many plants have also included programs for systematic study of the working environment in an attempt to control deleterious exposures, and others have established programs designed to diminish the time lost from general illness.

Many nonofficial agencies have of late become deeply interested in the problem of employee health. Some of these agencies, such as the Industrial Hygiene Foundation, are primarily supported by industry itself.

The federal government, of course, has been active in this field for many years. The division of industrial hygiene has been a part of the United States Public Health Service since 1914. Its functions include the co-ordination of all industrial-hygiene activities, both at federal and state levels, the promotion of industrial-hygiene service in state and local health departments, and investigations of a laboratory and field nature. These activities are conducted co-operatively with state

agencies, industry, labor, the medical profession and other professions and organizations.

The growth in the number of state health departments providing services in industrial hygiene has been almost phenomenal during the last five years, under the stimulation of funds provided by the Social Security Act. Today, there are thirty-four states with industrial-hygiene services, employing nearly two hundred and fifty professionally trained persons and spending approximately one million dollars for this activity.

In spite of all this progress, however, actually only a beginning has been made in providing adequate programs for the maintenance of employee health. The United States Public Health Service recently published the results of an analysis of a survey made in approximately 17,000 establishments employing 1,500,000 workers in fifteen representative states.<sup>1</sup> This analysis showed that only 15 per cent of the employees were provided with the services of full-time physicians, and that approximately 22 per cent were furnished the services of part-time physicians or physicians on call. These data are sufficiently representative to show that approximately two thirds of the workers in the United States are without any medical services at the plant proper.

Furthermore, the results of a recent study by the National Industrial Conference Board<sup>2</sup> indicated that in one third of the plants surveyed no efforts were made to supervise nonoccupational disabilities to assure the worker of medical attention. This study also showed that in only slightly more than half the plants was an effort made to promote employee health through educational means, and that only casual supervision was practiced over working conditions.

It may be assumed, therefore, that most industrial workers, when in need of medical services, receive them from the private practitioner—on a part-time basis at the plant, from physicians on call or from the family physician. It is a well-established fact, however, that the physician who spends but one or two hours a day in a plant, as well as the one who merely goes to the plant when called, has not the time to devote to a program of disease prevention.

This state of affairs, therefore, calls for serious consideration on the part of the medical profession regarding its responsibility in the vital field of industrial hygiene.

#### *Possible Contributions of the Physician*

It has been stated by authorities in industrial hygiene that the major needs are medical and surgical care to effect prompt restoration of health and earning capacity following disability, the pre-

vention of disability in industry by the proper control of the working environment and, finally, the promotion of health among workers. For those physicians holding positions in industry, and especially those completely responsible for furnishing programs of industrial-health maintenance, the Council on Industrial Health of the American Medical Association has suggested a definite procedure.<sup>3</sup>

This program consists in such functions as periodic inspection and appraisal of plant sanitation and occupational exposures, followed by the adoption and maintenance of adequate control measures. The provision of first-aid and emergency services and the prompt and early treatment of all illnesses resulting from occupational exposure are very significant functions of the medical department. Impartial health appraisals of all workers and provision of rehabilitation services for the correction of defects are additional functions of a medical department. And, finally, by means of recording and reducing absence due to all types of disability, it should be possible to make real progress in reducing lost time among workers, thereby not only benefiting the worker's physical well-being but also yielding tangible monetary advantages to both employer and employee.

The Council on Industrial Health of the American Medical Association has been very active in stimulating physicians, individually and through medical organizations, to contribute to the health of industrial workers. The council has also suggested the formation of committees on industrial hygiene in state and county medical organizations, and has clearly outlined a program that could be adopted by the state and local societies. The program of activities formulated for these committees comprises the following objectives: to train physicians to recognize and report occupational disease; to train industry and labor to the value of industrial health conservation; to elevate medical relations and standards under workmen's compensation; to scrutinize all social legislation affecting industrial health; to clarify relations between industrial and private practitioners; to improve relations between physicians and insurance companies; and to establish working relations with all state agencies interested in industrial health. I shall elaborate several of these objectives.

It is highly essential that physicians inform themselves further concerning occupational diseases, so that they may recognize such diseases more readily in the course of their practice. It would be advantageous for a private practitioner to make this effort, since he may be called on to

diagnose and treat such ailments in the course of his everyday practice.

It is pertinent to stress one other important item, namely, the necessity for obtaining an accurate and detailed occupational history. It is well known to what great lengths physicians go to obtain an accurate and detailed personal and past medical history of a patient, and yet they often neglect to obtain information concerning the patient's exposure to toxic materials in industry. Because a man's occupation may have a real bearing on his health, it is imperative that a history of his occupation be obtained in detail and interpreted properly. Such an inquiry may often necessitate investigating the patient's working environment or at least obtaining information on this point from the proper plant officials as well as from the patient himself. As an example of the advantage of the occupational history, a recent investigation by the United States Public Health Service indicates that manganese poisoning may often be mistaken for multiple sclerosis or Parkinson's disease.

With further reference to the subject of occupational diseases, it is obvious that unless the physician, whether he is in industry or in private practice, promptly reports to the proper authorities the occurrence of occupational diseases among workers, it will be next to impossible for the official agency responsible for the control of such diseases to carry out its functions. Physicians should adopt the same attitude toward the reporting of occupational diseases that now exists in the reporting of communicable diseases. The recurrence of such diseases may be prevented by a prompt investigation by a state industrial-hygiene service of the conditions in the plant that may include the causative agents. Once these have been established, prompt measures may be taken for the control of the environmental conditions responsible for the diseases.

In addition to these responsibilities, still another obligation should be given consideration. This deals with advising the individual patient regarding his health. The physician is the only one to offer such advice, and it is likely that he will have more success in doing so than anyone else. The patient's co-operation should be enlisted not only in the prevention and control of diseases arising out of the occupation, but also in the promotion of general health and mental well-being.

The physician can make still another important contribution to industrial medicine by stimulating pre-employment and periodic physical examina-

tions of workers in industry, and by calling attention to the necessity for correcting the physical defects revealed by health examinations.

I have repeatedly stressed the need for co-operating with the local health agencies, which are responsible for protecting the health of workers. The private practitioner, either as an individual or through his state or local medical organization, should utilize to the fullest extent the services that may be rendered by the official industrial-hygiene unit, and through it the facilities available in the entire health department. With the exception of Maine, all the New England States today have industrial-hygiene services. Services that may be rendered by the official agencies include: consultation with plant management regarding needed corrections of environmental conditions; advice to the management and medical supervisor concerning the relative toxicity of materials or processes, as well as that of new materials prior to their introduction into the industry; assistance in developing, maintaining and analyzing absentee records; consultant service to medical supervisors, private physicians, compensation authorities and other state agencies regarding illnesses affecting workers; provision of necessary laboratory service; and integration with other public-health bureaus in their programs for workers—for example, the control of cancer, syphilis and tuberculosis.

\* \* \*

I have attempted to define some of the problems of industrial hygiene, the methods employed in their solution and the opportunities that the physician has to make a real contribution toward the maintenance of employee health. I should like to commend to you the thought, expressed by Dr. C. D. Selby,<sup>4</sup> that every physician in industry should consider himself a health officer of that industry. As a matter of fact, I should like to go a bit farther and recommend this point of view not only to the industrial practitioner, but also to the private practitioner in his contact with the industrial patient. It is only by such an approach that progress will be made in efforts to conserve the health and efficiency of millions of workers.

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# CLINICAL CLASSIFICATION AND DIAGNOSIS OF HEMORRHAGIC DIATHESSES\*

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BOSTON

THE abnormal tendency to bleed has been a medical enigma for centuries, and only within the last few years has some semblance of order emerged from this hitherto chaotic field. Immediate and widespread practical application has followed recent advances in knowledge of the hemorrhagic diatheses, and although, as Nygaard<sup>1</sup> has pointed out, no accurate etiologic classification is at present available, from a clinical point of view it is essential to group these conditions into certain logical categories. In a series of 124 cases of various hemorrhagic disorders, an attempt is made to employ a classification that relates as closely as possible the etiologic and pathogenic factors to the clinical aspects of the disease. Moreover, on this basis, the diagnostic value of certain clinical and laboratory procedures is outlined.

## CLASSIFICATION OF HEMORRHAGIC DISORDERS

Hemorrhage may be considered to occur for only two fundamental reasons—either because of failure of the vascular integrity or because of a defective blood coagulating mechanism<sup>2</sup>; of course, the two conditions may coexist.

## Defective Vascular Integrity

It is customary to divide vascular disorders into nonthrombocytopenic and thrombocytopenic purpuras (Table 1). Unfortunately, owing to inadequate methods of clinical investigation, comparatively little is known about capillary bleeding.<sup>3,4</sup> It is well established, however, that unrelated to platelet deficiency the anatomic and functional integrity of the vascular endothelium can be adversely affected by a variety of agents, such as trauma, lack of vitamins C and P, and various toxic, allergic and metabolic processes. These so-called "capillary purpuras" form the largest group of hemorrhagic disorders, and Quick<sup>4</sup> and, more recently, Haden and Schneider<sup>5</sup> have pointed out that disorders of this type are more significant than coagulation defects from a practical standpoint. Little comment concerning this group is necessary. Subclinical scurvy is commoner than realized; toxic purpuras are of frequent occur-

rence, and if all cases with slight hemorrhagic tendencies were included, the group would be considerably larger. The diagnosis of these nonthrombocytopenic purpuras rests mainly on the history and the fact that clinical laboratory procedures are negative, with the exception of a positive capillary fragility test in certain cases.

Of much more serious implication are conditions in which capillary disturbance is associated with

TABLE 1. Hemorrhagic Disorders Characterized by Defective Vascular Integrity.

Etiology	Clinical Evidence	No. of Cases
<b>Nonthrombocytopenic purpura</b>		
Vitamin C (and P) deficiency	Scurvy	14
Chemical, bacterial or unknown toxin	Purpuras accompanying various intoxications	26
Allergy	Henoch's purpura and those of other types	2
Physical and metabolic defects	Purpura, following heat, cold, trauma, asphyxia and sclerosis	6
Congenital defects	Hereditary capillary telangiectasis	1
<b>Thrombocytopenic purpura</b>		
Secondary to toxic, allergic, chemical or physical agents depressing or invading the marrow	Purpuras accompanying leukemia, pernicious anemia, metastatic bone marrow lesions, aplastic anemia and benzol, x-ray and arphenamine poisoning	25
Idiopathic (splenic or megakaryocytic)	Essential purpura	5
Total		79

a decreased number of platelets. These may be subdivided into secondary and idiopathic thrombocytopenic purpuras. In the secondary type, the platelet reduction is due to depression or destruction of the marrow by toxic, allergic, chemical or physical agents. Severe purpuric manifestations are frequently encountered in leukemia and aplastic anemia. In this study of 41 cases of leukemia, hemorrhagic lesions developed in 16. Purpura of this type also occurs (but less frequently) in neoplastic metastasis to the bone marrow and in pernicious anemia.

The pathogenesis of idiopathic thrombocytopenic purpura remains obscure, owing to the lack of knowledge concerning the role of the platelets and the physiology of the capillaries. Wiseman, Doum and Wilson<sup>6</sup> state that the lack of platelets is the most significant and universal finding in this disorder. The cause of the thrombocytopenia has not been definitely established, but the likeliest

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theories are either that the spleen exerts an abnormal thrombocytolytic activity or that in some manner as yet unknown the spleen inhibits the production of platelets by the bone marrow. However, other investigators, especially Elliott,<sup>7</sup> emphasize the role of the capillary disturbance. Until further information is obtained concerning the relation of the platelets to the release of thromboplastin, to clot retraction and to capillary permeability, the problems involved in the etiology of essential purpura will remain unsolved.

Regardless of theoretical considerations, the differentiation of idiopathic and secondary thrombocytopenic purpura is an extremely vital matter. On the one hand, an ill-advised splenectomy will result in disaster, whereas in the properly selected case a dramatically successful cure will often be accomplished. Special emphasis should be placed on a careful history and physical examination, with particular attention directed toward uncovering possible etiologic factors, such as drug intoxication, allergy, infections and lesions involving the bone marrow. In both types of thrombocytopenic purpura, the bleeding time is usually prolonged, capillary resistance and platelets are markedly decreased, and clot retraction is poor or absent. The clotting time is usually normal but in severe thrombocytopenia may be prolonged, and Nygaard<sup>8</sup> points out that the plasma is usually hypocoagulable. Wiseman et al.,<sup>6</sup> in their excellent article, stress the facts that the spleen, liver and lymph nodes are not enlarged in idiopathic thrombocytopenic purpura, and that except for the diminished platelets, unless severe blood loss has occurred, the blood and bone marrow studies are not abnormal. Limarzi and Schleicher<sup>9</sup> strongly advocate bone-marrow studies, and most investigators agree that this procedure is essential before splenectomy.

### Defective Blood Coagulation

In considering the coagulation aspects of hemorrhagic disorders, Quick<sup>4</sup> points out that as a result of the researches of a number of workers a satisfactory hypothesis of the mechanism of blood coagulation is now available. Briefly stated, it is postulated that the plasma contains a protein substance of unknown composition called prothrombin, which is elaborated in the liver through the agency of vitamin K. When blood is shed, this inert substance is converted to thrombin by thromboplastin in the presence of ionized calcium. Thromboplastin is said to be a cephalin-protein complex normally found in the tissues and platelets. Recent work<sup>10</sup> indicates that a substance similar to tissue thromboplastin also exists in the

plasma. As a second phase, thrombin activates soluble fibrinogen to insoluble fibrin. Fibrin acquires the characteristics of adhesiveness, contractility and elasticity, forming the blood clot.<sup>11</sup> On the other hand, it is recognized that certain anticoagulants exist, and although the role of heparin is a matter of debate, it apparently activates the

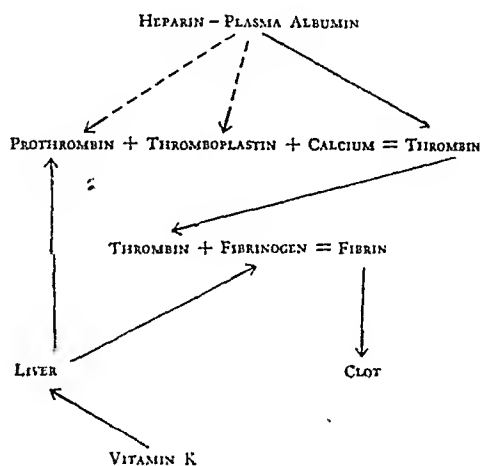


FIGURE 1. *Theory of Blood Coagulation.*

serum albumin to an antithrombic or antiprothrombic capacity.<sup>12</sup> Modified after Quick<sup>4</sup> and Eagle,<sup>13</sup> this theory is diagrammatically expressed in Figure 1.

It may be assumed that any anomaly of the clotting mechanism could result in a corresponding hemorrhagic disorder. Nevertheless, from a clinical standpoint, deficiencies of calcium are unknown, and acquired or congenital fibrinogenopenias are extremely rare.

Of great physiologic and clinical interest is the deficiency of thromboplastin. It is now fairly well established, in large measure owing to the work of Patek, Stetson, Taylor, Pohle and Lozner,<sup>14-16</sup> that hemophilia is caused by a lack of thromboplastin. It is still a controversial point whether this deficiency is caused by an intrinsic lack of a plasma thromboplastin or whether the lack of thromboplastin is due to the slow release from platelets that are abnormally resistant to disintegration. Hemophilia is infrequently encountered in practice, but the characteristic occurrence in the male, in addition to the usual hereditary features and the history of bleeding episodes, makes the diagnosis relatively obvious. Furthermore, the greatly prolonged clotting time associated with normal bleeding time, normal platelet count and clot retraction, prothrombin level and capillary resistance usually confirms the clinical diagnosis. Quick<sup>17</sup> recently pointed out that, in doubtful cases, study of the clotting time of recalcified plasma may yield valuable information.

Hypoprothrombinemia has assumed an increasingly significant clinical role since the advent of vitamin K and the simple laboratory tests for prothrombin. Such conditions are encountered with relative frequency, are usually easy to recognize, and for the most part are amenable to specific therapy. The lack of prothrombin is commonly associated with liver disorders, and it should be emphasized that vitamin K frequently has little effect on raising the prothrombin levels in the presence of continued liver damage. Twelve cases of hepatitis and cirrhosis in this series had intractable bleeding, uncontrolled by vitamin K. From the practical standpoint, the most serious and most commonly encountered hypoprothrombinemias are those due to deficiency of vitamin K either because of lack of absorption from the gastrointestinal tract, as in obstructive jaundice, bile fistula and bowel lesions, or from the dietary lack of vitamin K, especially in hypoprothrombinemia of the newborn.

In differentiating hemorrhagic disorders due to defective coagulation, it is essential, first of all, to

TABLE 2. Hemorrhagic Disorders Due to Defective Coagulation.<sup>4</sup>

ETIOLOGY	CLINICAL EVIDENCE	NO. OF CASES
Calcium deficiency	None known	0
Fibrinogen deficiency	Fibrinopenia	
Congenital	Congenital fibrinogenemia	6
Acquired	Severe liver damage and nutritional and bone marrow disturbances	0
Thromboplastin deficiency	Thromboplastinopenia	
Lack of plasma thromboplastin or faulty release of platelet thromboplastin	Hemophilia vera (2) and sporadic hemophilia (1)	3
Prothrombin deficiency	Hypothrombinemia	
Liver damage	Hepatitis and cirrhosis	12
Deficiency of vitamin K	Deficiency of vitamin K	
Lack of absorption	Obstructive jaundice, bile fistula and bowel disturbances	8
Dietary deficiency	Hypoprothrombinemia of newborn	19
	Total	42

suspect a real or potential lack of one of the constituents necessary for coagulation and, secondly, to investigate the degree and nature of the deficiency by proper laboratory methods (Table 2).

### Miscellaneous Disorders

Less well defined are a miscellaneous group of hemorrhagic states (Table 3) occupying a mid-zone between the capillary and clotting disorders, about which there is inadequate knowledge. These cases often have hereditary or familial characteristics, and various terms have been employed in

designating these disorders, such as hereditary hemorrhagic diathesis, pseudohemophilia and thrombasthenia. In this series, 3 cases were placed in this category. Usually, the clotting time, platelets and prothrombin levels are normal, but there may be prolonged bleeding time, poor clot retraction and decreased capillary resistance. Circulating anticoagulants, including the transitory phe-

TABLE 3. Miscellaneous Hemorrhagic Disorders.

ETIOLOGY	CLINICAL EVIDENCE	NO. OF CASES
Unclassified	Thrombasthenia	2
	Pseudohemophilia	1
Intrinsic fibrin defects	Lack of retraction, adhesion and elasticity	0
Presence of anticoagulants	Peptone and anaphylactic shock, unclassified types	0
	Total	3

nomena of peptone and anaphylactic shock, have been reported but are very rare. In this regard, the report of Lozner, Jolliffe and Taylor<sup>18</sup> on a case of a patient with a circulating unidentified anticoagulant is of considerable interest. Another somewhat neglected phase of the clotting mechanism that may markedly influence the occurrence of abnormal bleeding is that of syneresis or clot retraction.<sup>19</sup> Proper retraction, adhesiveness and elasticity are necessary for normal clot formation, and in addition to the physical role of the intact platelets in the clot structure, further study may indicate that the disintegrated platelet or other substances modify the intrinsic retractile properties of fibrin. A recent report by Rabinowitz<sup>20</sup> on the effect of methionine on clot retraction should arouse renewed interest in this aspect of the problem.

### LABORATORY PROCEDURES

In part, the confusion and obscurity attending the diagnosis of bleeding disorders has been due to the lack of application of uniform and relatively simple laboratory tests. Table 4 lists the nature and outcome of such procedures in the major hemorrhagic disorders.

In addition, complete blood studies, the Hinton test and urinalysis should be carried out routinely, as well as special determinations for vitamin C, calcium and fibrinogen when indicated. When performed accurately and subject to proper interpretation and when correlated to the clinical findings, these procedures, which are economically and technically available to practically everyone, should result in a correct diagnosis in all but a few of the most obscure hemorrhagic disorders.

## SUMMARY AND CONCLUSIONS

The various hemorrhagic disorders in the light of recent advances may be grouped into certain logical categories.

In establishing a diagnosis of abnormal bleeding, the value of a careful history and physical exam-

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TABLE 4. *Laboratory Procedures to Be Used in the Diagnosis of the Major Hemorrhagic Diseases.*

TEST	IDIOPATHIC THROMBO- CYTOPENIC PURPURA	CAPILLARY PURPURA	HEMOPHILIA	SEVERE HYPOTHROM- BEMIA
Bleeding time, Duke <sup>21</sup> (normal, 2-4 min)	Prolonged	Normal	Normal	Prolonged
Clotting time, Lee and White <sup>22</sup> (normal, 5-10 min)	Normal	Normal	Prolonged	Prolonged
Clot retraction (normal, complete in 1½ hr)	Poor	Normal	Normal	Poor
Platelet count (normal, 350,000)	Decreased	Normal	Normal	Normal
Capillary resistance	Poor	Normal or poor	Normal	Normal
Prothrombin clotting time, Quick <sup>23</sup>	Normal	Normal	Normal	Prolonged

ination related to certain laboratory procedures is stressed.

In this manner, in a series of 124 cases of various hemorrhagic disorders, satisfactory diagnoses were established and the proper treatments instituted in all but a few cases.

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## UNDULANT FEVER IN MASSACHUSETTS

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UNDULANT fever was recognized as a clinical entity by Marston<sup>1</sup> in 1861, and the etiologic agent was first observed by Bruce<sup>2</sup> in 1887. In 1897, the name "undulant fever" was given to the disease by Hughes<sup>3</sup>, and in 1905 the goat was found to be the reservoir by Zammit,<sup>4</sup> of the British Commission working in Malta. In the same year, Craig<sup>5</sup> reported the first authentic case of brucellosis in the United States, but the first intimation that the disease was endemic in this country came with the work of Ferenbaugh<sup>6</sup> in Texas in 1911. Some years elapsed before cases were recognized with regularity in New England, but since 1928 the Massachusetts Department of Public Health has been keeping individual epidemiologic records of the disease. Although it was not made reportable until 1930, an occasional case history was obtained in years previous to that time 14 such case histories being on file.

Since the disease was made reportable, 331 cases have been recorded through 1940. Until 1934, no more than 15 cases were recorded in a single year, but after that time more than 40 cases were reported in most years: 1935, 42 cases; 1936, 55; 1937, 43; 1938, 37; 1939, 40, and 1940, 52. No doubt, the principal reason why the number of cases has become higher is that physicians have become more alert in suspecting the disease. This is evidenced by the increase in the number of specimens sent to the State Laboratory for undulant fever agglutination tests. From 1929 through 1940, the numbers of specimens examined in successive years were 167, 280, 401, 339, 374, 457, 742, 1105, 1393, 1871, 1933 and 1996. It must be realized that these figures include a large number of duplicate specimens on the same persons, because in some cases the diagnosis was partly dependent on an increasing titer of agglutination.

It was believed that a summary of the information contained in the epidemiologic records accumulated by the department would be of interest to physicians of the State. In all, 337 histories have been obtained from the 345 cases that have come to our attention since 1927.

It should be pointed out that the information is not at all comparable with that which would be available from hospital records, since in many

cases details are somewhat sketchy, partly because the histories were frequently obtained as soon as the disease was suspected and before all the characteristic symptoms had occurred, and partly because the patients had been seen by several physicians, no one of whom had all the details of the illness. It should also be borne in mind that the primary purpose of the records was to aid in deciding whether the case was really undulant fever, and when it appeared that the diagnosis was justified no further details seemed to be needed.

The inadequacy of the information in these epidemiologic records is indicated by the fact that, after the information available regarding the symptoms, the course of the disease and the laboratory work had been considered, in only 160 cases (48 per cent) was the diagnosis unequivocally justified. On 104 cases (31 per cent), information was less adequate, but it appeared that the disease was probably undulant fever. In 47 cases (14 per cent), from the details available, there seemed to be a possibility that the disease was undulant fever, whereas in 26 cases (8 per cent) information was so inadequate that no opinion was ventured.

*Seasonal Prevalence*

The Mediterranean type of undulant fever in Malta is usually most prevalent in the summer. In Massachusetts, where the disease is largely due to *Brucella abortus* instead of *B. melitensis*, there is very little tendency toward predominance in any season, the cases being fairly evenly distributed throughout the twelve months—January, 29 cases; February, 17; March, 25; April, 24; May, 30; June, 28; July, 27; August, 28; September, 23; October, 36; November, 32, and December, 32.

*Age and Sex Distribution*

On the Island of Malta, the sexes are apparently about equally involved by undulant fever, but in this country there has always been a predominance of males. In our cases, there were 199 cases among males and 85 among females. The comparative rarity of reported cases in the young is likewise borne out by our figures, only 6 per cent of the cases occurring under ten years of age and less than 11 per cent of the total cases between ten and nineteen, whereas each decade thereafter shows approximately double that percentage.

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Occupation

In contrast to the observations of Hardy et al.,<sup>7</sup> who found that packing-house employees and workers on farms in Iowa were more frequently attacked, in Massachusetts only 4 of the 270 patients whose occupations were specified were meat handlers; 19 were engaged in farming, and 14 in dairying. The groups most frequently attacked comprise perhaps the largest portion of the population in the State, such as persons engaged in housework, mechanical workers, students, factory workers and clerical workers. This indicates that the method of transmission in Massachusetts may be materially different from that in Iowa. The distribution is one that would be expected if the disease were transmitted by drinking milk.

Fifty-two persons were reported to have had direct contact with cows. In 36 cases, it was not stated whether this was more than the occasional contact of living on a place where cows were kept. In 8 cases, the patient was said to have milked cows, and 8 other patients took care of an aborting cow. Only 1 person was noted to have been in contact with goats alone, and 6 with pigs alone. Undoubtedly, a number of the 52 patients who had been in contact with cows also came in contact with pigs, and a few may have been in contact with goats. However, except for the 8 who were in contact with aborting cows, the disease may very well have been contracted through the drinking of milk rather than by contact with animals.

Prevalence in Urban and Rural Groups

When the cases are tabulated according to the size of the community, it becomes apparent that the smaller the city or town, the higher the rate of undulant fever (Table 1). This distribution of

TABLE 1. *Distribution of Undulant Fever by Size of Community (Massachusetts, 1931-1940).*

POPULATION	NUMBER OF CASES	ANNUAL RATE PER 100,000 POPULATION	PERCENTAGE OF MILK PASTEURIZED
Over 25,000	85	0.3	98.3
10,000-25,000	90	1.2	78.2
5000-10,000	47	1.4	65.0
2500-5000	47	2.4	58.5
Under 2500	56	2.8	?
	325	0.8	85.9

the cases is, of course, also inversely proportional to the use of pasteurized milk, since the smaller the community, the smaller the amount of pasteurized milk used. This points very strongly to raw milk as the source of the disease, which is in line with what would be expected in view of the fact that one sixth of the dairy cattle in Massachusetts are probably infected with Bang's disease.

The same relation is seen when the cases are tabulated by counties. The more rural the county

TABLE 2. *Distribution of Undulant Fever by Counties (Massachusetts, 1931-1940).*

COUNTY	*NO. OF CASES			ANNUAL RATE PER 100,000 POPULATION	PERCENTAGE OF MILK PASTEURIZED
	1931-35	1936-40	TOTAL		
Barnstable	0	4	4	1.1	71.4
Berkshire	12	37	49	4.1	47.1
Bristol	6	15	21	0.5	77.5
Dukes*	1	2	3	3.3	22.0
Essex	8	18	26	0.6	88.1
Franklin	9	12	21	4.0	51.5
Hampden	3	13	16	0.6	90.5
Hampshire	6	5	11	1.4	48.7
Middlesex	13	25	38	0.4	96.4
Norfolk	7	13	20	0.6	86.1
Plymouth	4	14	18	1.2	70.7
Suffolk	3	5	8	0.1	99.8
Worcester	26	64	90	1.8	71.7
	98	227	325	0.8	86.4

\*Including Nantucket.

and the less the amount of pasteurized milk used, the higher the rate of undulant fever (Table 2).

Symptoms

The six chief symptoms are listed in Table 3. Fever was the most prominent one, being recorded in 84 per cent of the 272 cases in which symptoms

TABLE 3. *Frequency of Symptoms by Sex.*

SYMPTOM	MALES		FEMALES		TOTAL	
	NO. OF CASES	PER CENT	NO. OF CASES	PER CENT	NO. OF CASES	PER CENT
Fever	162	87	65	76	227	84
Chills	86	46	43	50	129	48
Sweats	86	46	27	31	113	42
Weakness	71	38	34	40	105	39
Headache	58	31	22	26	80	29
General aches	44	24	15	18	59	22

were recorded. Chills occurred in nearly half the cases, and sweats and weakness were present in about 40 per cent. The only other prominent symptom was a complaint of general aches, including pains in the joints, muscles, back, neck and shoulders.

Among the many other symptoms mentioned, some were no doubt associated with the brucellar infection, but others may have been due to coincidental conditions. These symptoms, in order of frequency, were: malaise, 43 cases; loss of appetite, 34; loss of weight, 28; nausea, 19; listlessness, 17; abdominal pain, 12; vomiting, 7. Dizziness, restlessness, insomnia, prostration, diarrhea, cough, dyspnea and a few other symptoms were mentioned occasionally.

An attempt was made to estimate the severity of the symptoms. Nearly three quarters of the cases appeared to be moderate in severity, less than 10 per cent were severe, and the remainder

were mild or subclinical. Symptoms were slightly milder in females than in males. Age seemed to have little influence on severity except that, in patients under ten years of age, the cases tended to be either mild or severe, the proportion of moderately severe cases decreasing to less than 50 per cent; in the older ages, about 75 per cent of the cases were moderately severe.

Another criterion of the severity is the delay in the discovery of the cases as measured by the time elapsing from the onset of symptoms to the reporting of the case. One would expect that the milder the symptoms the greater the delay. Nearly half the cases were not reported until from one to three months after onset, and in about one eighth the delay was even longer. The fact that among females there was a longer delay after the fourth week indicates either that the symptoms were milder or that the infection was more frequently confused with some other disease in that sex.

#### *Agglutination Tests*

Of the 178 cases in which the results of agglutination tests were recorded, 109 showed positive reactions in dilutions from 1:135 to 1:1215 inclusive; 44 showed positive reactions in dilutions greater than 1:1215, whereas only 6 showed positive reactions in dilutions less than 1:135. In 19 cases, it was stated merely that the agglutination was positive, and no titer was given. There was no significant difference in the distribution of these varying degrees of agglutination by age. In 169 cases, it was possible to estimate the time that elapsed between the onset and the last test performed. Two patients in whom the titer was less than 1:135 were tested only early in the disease. As would be expected, those in whom the last test was less than four weeks after the onset of the disease tended to have titers somewhat lower than those in whom the last test was made after that time. There was no marked difference in agglutination tests in the two sexes.

#### *Probable Source of Infection*

It has already been noted that only a few cases can be explained by direct contact with infected animals. For this reason, considerable attention was directed to the source of the milk supply of those who became ill. Table 4 gives the kind of milk that was used regularly. It will be noted that almost 80 per cent of the patients gave a history of using raw milk regularly, less than 10 per cent used pasteurized milk regularly, and about 11 per cent made no statement about the regular milk supply. Many of these patients, in addition

to using milk from their regular supply, obtained milk on occasion from other sources. Twenty-five per cent of those who had a secondary milk supply used raw milk either occasionally or frequently.

An analysis of the 32 cases in persons who claimed that their primary milk was pasteurized is illuminating. Fourteen of these obtained raw

TABLE 4. *Kind of Milk Used Regularly in Reported Cases of Undulant Fever.*

KIND OF MILK	NO. OF CASES	PER CENT
Raw	215	63.8
Raw and pasteurized	52	15.4
Pasteurized	32	9.5
Not stated	38	11.3
	337	

milk from secondary sources, 7 frequently and 7 occasionally. Eleven of the remaining 18 were recorded as not having used any raw milk. Of these, 2 had handled aborting cows, 3 had handled carcasses of animals, 1 worked at a piggery where other cases of undulant fever had occurred, 1 had no symptoms, and 1 showed a positive agglutination reaction after a skin test had been performed; in the remaining 3, there was suspicion that raw milk had been used. Seven of the 18 histories contained no statement concerning a secondary milk supply. Of these, 3 patients were in contact with cows or pigs, 2 may have become infected from cheese, the diagnosis was questionable in 1 case, and the last patient probably used some raw milk.

An analysis of the 38 cases in which there was no statement about the primary milk supply is also of interest. Fifteen of these patients lived in communities in which pasteurized milk was not regularly available, and it is logical to conclude that they used raw milk. Eight others used raw milk from secondary sources. Two had handled aborting cows, 1 was a laboratory infection, 5 had no record of a confirming agglutination test, and in the remaining 7 the use of raw milk could be neither excluded nor verified.

In many cases, information was collected about the dairy herds when a raw milk supply was involved. Records concerning 93 herds in which abortus testing had been done were available. Eighty-six of these herds showed reactors, only 7 being entirely free of Bang's disease. In 175 cases, there was a statement of whether abortions had occurred in the herd; in 76 (44 per cent), the answer was in the affirmative.

### *Relation of Prevalence of Undulant Fever To Milk Regulations*

Since undulant fever was not recognized in Massachusetts before about 1920 and was not recorded regularly until after 1930, it is impossible to submit statistics to show whether the disease has been increasing or decreasing. It is believed, however, that the prevalence of undulant fever has declined in the same manner as that of other milk-borne diseases as the quality and safety of milk supplies have improved.

The great impetus to place safeguards around milk in Massachusetts was given by the epidemics of milk-borne septic sore throat that were striking one community after another in the years immediately following 1911. The use of pasteurized milk increased progressively, occasional outbreaks of milk-borne diphtheria, scarlet fever and typhoid fever giving further emphasis to the need for such safeguards. The large outbreak of nearly 1000 cases of septic sore throat, with 48 deaths, in Lee in 1928, however, initiated action by local boards of health to require pasteurization or certification of all milk sold. Beginning with Boston in that year, one after another of the communities in the State have required that only safe milk may be sold, until at the present time seventy-seven communities, representing almost 80 per cent of the population, have regulations requiring pasteurization or certification of all milk sold.

The number of outbreaks traced to milk has progressively decreased with the increased use of pasteurized milk. From a peak of forty-five outbreaks, with 4255 cases, in the five-year period 1911-1915, the number has dropped to 4 outbreaks, with 331 cases, in the five-year period 1936-1940. No deaths have resulted from epidemics of milk-borne disease in the last five years. No cases of diphtheria have been traced to milk since 1925; the last milk-borne outbreak of typhoid fever occurred in 1932; and the last scarlet-fever outbreak due to milk was in 1933. The outbreaks during the last five years were due to streptococcal sore throat and undulant fever, all on raw-milk routes.

It is estimated that almost 90 per cent of the milk sold in the State is now pasteurized. Other communities are expected to pass regulations requiring pasteurization or certification in the near future, making the prospects good for a further decrease in milk-borne disease.

### SUMMARY AND CONCLUSIONS

A summary is given of 337 epidemiologic case records from 345 cases of undulant fever in Massachusetts occurring since 1927.

The number of cases reported has increased, probably owing to an increased alertness of physicians in recognizing the disease. The number of agglutination tests for undulant fever performed by the State Laboratory has rapidly increased.

There is little tendency for cases to predominate in any season.

The age and sex distributions parallel those reported from other parts of this country.

Danger of infection is not limited to any particular occupation in Massachusetts.

The disease is most prevalent in rural areas where little pasteurized milk is sold.

Most of those ill of the disease give a history of the use of raw milk, either regularly or occasionally.

With almost 80 per cent of the population of the State living in communities requiring pasteurization or certification of all milk sold and with almost 90 per cent of the milk consumed already pasteurized, milk-borne disease can be expected to remain at a low level.

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## COMMUNITY SUPERVISION OF MENTAL DEFECTIVES IN MASSACHUSETTS\*

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BOSTON

FOR many years, mentally defective children have been referred to as "institutional problems." This belief has come into being since 1848, when the first state school was opened in Massachusetts. Quite commonly, physicians, nurses, social agencies and practically all social workers have as sociated mental deficiency with institutional placement. The resultant concentrated demand has created crowded state schools and long waiting lists. With institutional care as the advocated and generally accepted solution of the problem, the possibilities of community adjustment of mental defectives have received scant attention. Paradoxically, this situation has come about in spite of the fact that community supervision by parents, and satisfactory supervision in all but a few cases, had been going on long before the establishment of state schools. What is the history of community supervision, and what are the possibilities of community adjustment of mental defectives? Is there any other answer than institutional care for cases of mental deficiency?

In 1915, the state schools of Massachusetts<sup>1</sup> began to experiment with the thought of placing trained boys and girls in the community at wages. This was started with some diffidence since, up to that time, there had been a rather firm belief that mental deficiency was a permanent institutional problem. In fact, the late Dr. Walter E. Fernald once said that no mental defective should be released from a state school. After he saw some of the work being done at the Wrentham State School by Dr. George L. Wallace, he<sup>2</sup> had an extensive study made of the outcome of boys and girls who had left his school at Waverley and returned to the community. These children had been removed from the school against Dr. Fernald's advice. He found that many had turned out favorably, and that his pessimistic predictions of earlier years had not been justified.

For the last twenty-five years, state schools have conducted a parole program for girls and boys who have been able to profit by the training offered by the schools. They are placed in paying positions in the community and are supervised by

the social workers of the respective schools. At the end of 1940, 233 girls and 106 boys were on parole from the Fernald, Wrentham and Belcher-town state schools. The 339 on parole earned a total of \$45,747.84 during 1940. This is an average of \$134.95 for each, or an average weekly wage of \$2.60 in addition to maintenance. This amount is not large, but when one realizes the rather limited accomplishments of many of these boys and girls, it is not unreasonable. The main thought to be preserved is that children once considered total losses economically and socially, because of mental deficiency, have now been made into self-supporting citizens. Monthly checking by the social workers of working and living conditions, wages received and other financial exchanges between employer and employee obviates exploitation.

During the last fifteen years, however, another type of community supervision has come into being. The overcrowding of the three state schools has made it impossible for children seeking admission to receive the desired training in such a school. Complicated social problems and difficult home situations have been observed in many of these children. There is urgent need for early admission, but the impossibility of admitting more children to already overcrowded buildings is obvious. In this situation, it has become necessary that the Department of Mental Health take some means to offer at least temporary relief. The suggestion for a plan of community supervision by the department came from Dr. Fernald himself, thus showing the willingness of a great man to reverse a former decision. In 1921, Dr. Fernald in collaboration with Dr. George M. Kline, at that time the Commissioner of Mental Diseases, elaborated the statute (Section 66A, Chapter 123, of the General Laws) that legalizes the commitment of feeble-minded persons to the department for community supervision. The original bill was amended in 1924, when the division of mental deficiency, whose personnel comprised a psychiatrist, two social workers and one stenographer, was created within the central department. Since then, the number of social workers has been increased to three. From time to time, the supervisory work has been expanded, developed and

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altered to meet the new and changing needs of the community.

Mentally defective children are referred for supervision by public and private agencies, as well as by individuals. The patients carried by the division fall into six general groups. In the following discussion, the different groups are arranged in accordance with the ages at which the patients are referred, the youngest being considered first.

#### GROUPS OF PATIENTS

##### *Home-Training Group*

The home-training children are the youngest placed under our care. They include children of preschool or school age, with mental ages from two years or less to about six years. Because of their low mentality, these children have been refused admission to school, or have been excluded from regular classes or special classes. They are at home without anything to occupy their time, and the parents need advice and help in providing necessary training. In other situations, children are awaiting admission to a state school. Owing to overcrowded conditions and the resulting long waiting lists, immediate admission is not possible. Thus, some definite plan to promote the adjustment of the child in his own home is urgently necessary.

Since 1937, home training and teaching lessons have been provided to aid these children. Outlined lessons and materials have been prepared for the following three classifications: Group A, mental age less than two years; Group B, mental age two to four years; Group C, mental age four to six years. A complete psychologic and mental examination is obtained early, since it aids the worker in assigning lessons and materials suitable to the mental age of the individual child. The social worker visits the home each month, and outlines and teaches a new lesson to the child and the mother. The parent then continues the lesson work for an hour or two each day. The successive lessons that make up the child's "school book" are printed on paper of different color and used primarily as a teaching aid for the parents. The attractive colored materials for the carrying out of each part of the lesson are provided at a minimum cost to the parents, or are supplied gratis if circumstances warrant.<sup>3</sup>

After learning to do simple handwork suited to his mental age, the child gains proficiency and is able to occupy himself in a constructive manner. He soon reacts to success in these tasks and almost invariably becomes a better adjusted member of the family group. In addition, the teaching of the lesson work by the parents often gives them their first real understanding of their child's mentality.

From that point on, they begin to plan for him on his own mental level. During the visits, the parents have frequent opportunities to discuss with the social worker any problems or conflicts arising in connection with the adjustment of a mentally deficient child. Institutionalization of many children has been postponed. As the child becomes adjusted in the home, the parents show less interest in placing him in an institution. In several cases, children previously excluded from school have shown great progress. After one or two years of home-training lessons, during which they have learned color, numbers, letters and simple school work, some of these children have improved so much that they have been able to return to special classes and remain in school indefinitely. About 55 of these boys and girls are being supervised by the division, and the referrals to this particular group are increasing each year.

##### *Special-Class Group*

The special-class group comprises children now being cared for within the public-school system. After examination by a traveling school clinic, the psychiatrist in charge may recommend special-class placement and social supervision. The divisional social workers visit the home and explain to the parents the difficulties experienced by the child in school and the advantages offered by the special class. In this way, the parents gain an understanding of the value of special-class training and how it may influence the development of work aptitudes on the part of the child. Very often, the parents have many other questions and problems to discuss with the social worker. Recreation, summer-camp placement, medical care and other assistance are included in the supervision of these boys and girls when the parents cannot arrange for them.

With older children attending special classes, analyses are made by the social worker and school teacher to plan vocational training and placement. After leaving the special class, the patient may be carried for supervision or placed in a training home. The child may be discharged if it is known that he is being satisfactorily cared for by the family or an agency.

##### *Training-Home Group*

Cases placed in training homes prior to wage placement are made up of girls seventeen to twenty-five years of age who have reached their capacity in regular-class or special-class work. The intelligence quotient ranges from 58 to 69. Some have been removed from unfavorable homes and environments, have no parents, and are under the complete care of the Department of Mental Health

as committed cases (Chapter 123, Section 66A, of the General Laws). Others have interested parents who pay all expenses incurred by their daughters in the training home, and are classified as voluntary cases. The training-home supervision and the medical, dental and recreational care are the same for both groups. The girls are placed in carefully selected and thoroughly investigated homes with an understanding foster mother who gives special instruction in housework, care of children, cooking and general training. The goal of future wage placement is emphasized at all times.

The social worker and the foster mother plan a course of training, which is carried out daily in the home. The progress and failures of the girls are checked frequently by the social worker through interviews. At regular intervals, the girls are instructed to make a record of their daily duties. Their accomplishments, attitudes, general appearance, conduct and progress, as well as their failures, are noted by the foster mother on the same report. In this way, knowledge of their efficiency and progress is gained and recorded. The girls are encouraged to attend church, 4-H clubs and suitable community activities where understanding persons are in charge. Protection and good influence are very valuable for retarded girls of these ages, since they are very impressionable and show the same response to either constructive or destructive influences. Under the present plan, two or three girls are placed in a training home, and a definite schedule of training for each is worked out with the foster mother. With frequent check-ups, the social worker can evaluate progress and judge how soon the girl will be ready for placement in a wage home.

The training requires from six months to two years, depending on the mental level of the patient. The annual expense of about \$350 is small if one considers that the training makes a self-supporting worker out of a potential dependent. To date, there has been a greater demand for girls trained in housework than the division could supply. As soon as a girl learns the basic routine in a training home, it is almost certain that there will be a suitable home waiting for her in the community.

#### *Wage-Earning Group*

The cases in the wage-earning group have comprised the principal type of supervisory work since the beginning of the division. Until recently, there were no funds for training potential wage earners. As a consequence, only retarded young women who gave indication of their ability

to work and support themselves could be accepted for supervision. These women are usually from twenty-one to thirty years of age, with an intelligence quotient ranging from 60 to 69. They are accepted as either committed or voluntary cases, depending on their background and circumstances. After a thorough investigation, the woman is placed at wages in a home in which it is thought that the employer and other circumstances will favor adjustment. She receives room, board and wages commensurate with her ability. Some have begun with wages as low as \$1.00 a week and progressed to \$8.00 a week. The average wage is between \$3.00 and \$4.50 a week. At the outset, the employer is informed frankly of the young woman's characteristics, plus or minus. She is also instructed in the art of dealing with the mentally deficient, if it happens that she has not had previous experience with them. She is told also of the part the employer must play in the supervision program and the regulations required by the department.

Each month, the employer returns to the division a wage report, which has been signed by the woman. This states the employee's wages, the weekly spending money given to her and the remaining amount sent in for banking. Her banking and purchases of clothing, and her medical, dental and recreational care are supervised by the social worker, who makes frequent visits to the employer and the employee to discuss any problems that may come up. In some cases, it has been necessary to make changes after a time and place the woman in a new working home. In these cases, another young woman is placed with the original employer. Most of these changes have worked out to the advantage of both the employer and the employee.

Experience with the wage-earning group has taught us that mental defectives, with supervision, can be influenced to carry on in the community as responsible, self-supporting citizens. Without guidance, they are easily swayed by doubtful influences and may become community responsibilities rather than assets.

#### *Family-Care Group*

The boarding-out or family-care cases have been placed by the division since 1938, when funds were appropriated for this purpose. Board is paid for two different types of patients: those who are potential wage earners and have already been described in the group trained in homes prior to wage placement; and those who constitute typical institutional cases of the lower mental ratings, with no ability for work training. Because of the overcrowded conditions of the state schools,

it has been necessary to provide boarding care for a few girls on the waiting list who cannot be continued in their homes. Surprisingly, it has been found that certain mental defectives may become satisfactorily adjusted in another home, although they were making no progress whatever in their own homes. In general, boarding care is less expensive than state-school maintenance, although the margin is not great.\* If the patient is committed to the department, the State pays the board. If the commitment is voluntary, the board is paid by relatives. In either event, the social worker investigates possible homes and selects the one considered most suitable for the patient. The foster mother is told frankly about the type of patient who is to be placed with her, and is given full opportunity to decide whether she desires to assume such a responsibility.

After a patient is placed in a home, the social worker visits frequently to aid the patient in adjusting herself to the new surroundings, and to assist the foster mother in understanding and dealing with the many problems associated with the mentally deficient. The patient's medical and dental care, clothing and recreation are supervised by the social worker. Arrangements have been made with state hospitals near the boarding homes for the patients' medical and dental care and for their attendance at church services and recreational programs.

The patients placed out during the last two years have been those of the imbecile level, with intelligence quotients between 35 and 49. Chronologically their ages have been from sixteen to sixty-eight years. For example, a girl sixteen years of age could not adjust herself to her own home, and institutional care seemed imperative. Because the state schools had no space available, the division was asked to find a suitable home. The board and all expenses were paid by her family. She has made a good adjustment in a quiet home with an understanding and patient foster mother. Two men, both sixty-eight years of age, who had been in a state school for over forty years, were transferred to the division and placed on a farm where their board was paid by the State. Both men have intelligence quotients around 50 and enjoy little duties, such as feeding chickens and simple chores. They have made a good adjustment in their new homes and are extremely happy. One wonders whether or not the forty years within an institution were necessary.

Although the boarding-out plan is a new ven-

ture for the division, it has been very successful. Overcrowded state institutions and long waiting lists demand an answer. Patients who have benefited from years of training and discipline at a state school but are not suitable for wage placements do very well. This is not only a very happy change for the patient but also effects a small saving for the State. In other cases, mental defectives who are poorly adjusted in their own homes because of unalterable circumstances make unexpected adjustments in foster homes. The family-care plan lessens the expense to the State and makes room in the schools for patients who cannot be cared for except by institutionalization.†

#### *General Supervision and Consultation Group*

The general supervision and consultation cases are referred by various public and private agencies as well as by individuals. The patients under general supervision are often older boys and girls who do not classify in any of the other five groups. Usually, they are being cared for in their own homes. Their parents or relatives are able to take care of their physical needs, but require guidance and assistance from time to time in dealing with the difficulties and problems associated with mentally deficient children or adults. Even an occasional contact with the patient and his family has been found to have a stabilizing effect on the family situation.

Consultation cases are those in which the division acts as an adviser to the referring agency or family. After investigation, the patient may be found to be suitable for supervision in one of the five groups already described. On the other hand, by reason of legal and financial limitations, the division cannot assume the care of certain types of cases, such as defective delinquents, patients incapacitated by severe physical infirmities and patients suffering from mental disease. Anyone referring such cases is directed to organizations that deal with these specific types. Likewise, cases of extreme mental deficiency, which cannot be supervised in the community by the division, are referred to state schools as urgent institutional cases.

Many family and children's agencies recognize mentally deficient cases among their clients and seek advice from the division. First, a complete mental and physical examination is made. A complete picture of the patient is arrived at by means of social and educational investigations, and also by physical, mental and psychological examinations.

†Family care from a state school was placed in operation in 1938, by Dr. George E. McPherson, superintendent of the Belchertown State School. About 50 older patients are being carried in suitable homes in the community. The beds vacated thus become available for younger and trainable patients on the waiting list. This service is in addition to the usual parole placements at wages being carried out at Belchertown.

\*The annual expense (\$350) for boarding care may be analyzed as follows: board, \$234; medical and dental care, clothing and so forth, \$90; social supervision, \$26. Annual charges for maintenance for 1940 in state schools were \$363 per patient.



After this procedure, the diagnosis, prognosis and course of action are summed up and discussed at a staff meeting. The referring agency is often willing to carry on the supervision if it may consult the division from time to time. The division co-operates with many community social agencies, schools, churches and clubs, and with individuals who seek advice about mentally deficient children or adults.

#### LEGAL STATUS OF CASES UNDER SUPERVISION

Committed and voluntary status has been mentioned in describing the different placement groups. When the department indicates its approval, any mentally deficient person may be committed to the Division of Mental Deficiency for supervision.\* The six types of cases outlined previously may be supervised on the voluntary status, but ordinarily the committed cases are placed in training homes prior to wage placement, in the wage earning group or the boarding out or family care group. The Division of Mental Deficiency, by law, has the complete care and supervision of the patient, including supervision of the patient's funds. In most cases, commitment is used because the patient has no suitable person to look out for his welfare. If he is under the family care plan, his board and maintenance are paid by the State. However, the majority of the committed cases are self-supporting. The voluntary cases usually have relatives who are able to take the financial responsibility but need assistance in the care and supervision of the patient in the community.

#### COMMENT

The six classifications of cases supervised by the division show the scope of work being done for the 300 cases of mental deficiency supervised in the community. In the early stages of this work, about fifteen years ago, mental deficiency was not recognized so promptly as it is at the present time. The examinations and diagnoses of mental deficiency by the traveling school clinics by the outpatient clinics of the state mental hospitals and schools and by the habit clinics have brought

about a growing awareness among private and public agencies, as well as the general community, of the problems of mental deficiency. Consequently, younger patients are being referred to state schools, clinics and to the Division of Mental Deficiency each year. The shift in type of case referred has changed the emphasis to supervision of the younger mentally deficient. In many cases, early recognition of the condition and helping parents to understand their retarded child have effected a satisfactory adjustment of the child in his own home and have indefinitely postponed institutional placement. When home adjustment is impossible, training homes and boarding homes have proved to be satisfactory as well as economical, and have taken some of the burden that previously went to the institutions.

When one realizes the growing number of recognized mentally deficient persons, it seems altogether reasonable that every possible plan be made to start the training of this group at an early age so that the number of maladjusted mental defectives may be kept at a minimum. Public and private agencies are showing an increasing interest in arriving at a complete understanding of this problem. The assistance they can offer should be developed to the greatest degree, since the care of mental defectives must become more of a community responsibility as time goes on. At the end of 1940, a total of over 54,000 mental defectives were known to the Department of Mental Health, through its Central Registry of Mental Defectives. Over 4,000 new cases of mental deficiency are being discovered each year. The Commonwealth can never assume the cost of providing institutional care for all this group. Many mental defectives require institutional care, but that is not the answer to the problem of mental deficiency, taken as a whole. The development and success of community supervision of mental defectives have proved its practicability. An increase in the personnel of the Division of Mental Deficiency is urgently needed to extend the work on a state wide basis. The Commonwealth should do everything possible to assist mentally deficient persons to a satisfactory social and economic adjustment in the home and in the community. Institutionalization should be the last thought, after all other resources have been exhausted.

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\*Sec on Gen. Chapter 123 of the General Laws reads: "Commitment to Department. If an alleged feeble-minded person is found upon examination by a physician qualified as provided by section fifty-three to be a proper subject for commitment, the judge of probate for the county in which such person resides or is found may upon application commit him to the custody or supervision of the department, but no person shall be so committed unless the approval of the department shall be filed with the application for the commitment. If he is committed to the custody or supervision of the department, the department shall thereafter have power whenever advisable to transfer him to a state school for feeble-minded or may cause an application to be made for his removal to a department for defective delinquents and such person may be so removed in the manner provided by section one hundred and sixteen. If the alleged feeble-minded person is committed to the custody or supervision of the department of mental diseases, the said department may temporarily release him in the manner provided by and subject to the provisions of section eighty-eight, or may discharge him under section eighty-nine."

DIABETES INSIPIDUS IN ONE OF TWINS\*

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BOSTON

IN the course of an investigation of a group of 30 patients with diabetes insipidus, I found that one patient, now an eighteen-year-old boy, had a nonidentical twin sister who did not have this disease. The twins differed so markedly in stature, general configuration and progress of growth that it appeared of interest to present their cases.

CASE REPORTS

*John's history.* John has had diabetes insipidus since the age of 5½ years, and I have observed him for the past 7 years. He was born 10 minutes before his twin sister. He and his twin each weighed 7 pounds at birth and were of normal height. The delivery, like the pregnancy, was normal and was performed at home without instruments. The patient had a healthy infancy and gained moderately well. He has had a pigeon breast since birth; he was given cod-liver oil from the age of 3 months, and orange juice until he was 3 years old. He developed his first tooth at 6 months and walked at 15

had become deeper, and there was a beginning growth of hair on the face and a considerable growth of pubic hair, although it had a female distribution. The penis was 5 inches long, and he had daily erections; the testes, too, were normal in size.

Physical examination was not remarkable, except for stunted growth. The basal metabolic rate was -9 per cent at the age of 14 years.

The laboratory data are given in Table 1.

*Joan's history.* Joan's birth was normal, and she had a healthy childhood and normal subsequent maturity. She had a normal growth, unlike her twin brother. She is now a tall, well-built and attractive girl. She was bright at school and graduated from high school at the age of 17 years. She has a pleasant personality, in contrast to John. During her childhood, she had much the same diet as her twin brother.

The menses began at the age of 13 years, and they have been regular and normal since then. The basal metabolic rate was -19 per cent at the age of 14 years. Physical examination is entirely negative.

*Family histories.* The father, mother, three brothers and one sister appear to be well and normally developed. There is no history of diabetes.

*Comparative physical characteristics of the twins.* The difference in the general appearance of these twins has been striking, as illustrated in Figure 1. Joan, at the age of 18 years, is a well-developed, mature girl who is about a head taller and 25 pounds heavier than John, who appears stunted in growth and underdeveloped.

Table 2 presents a record of the progress of the twins' height and weight at intervals of approximately 1 year.

*Comparative x-ray studies of twins.* When the twins were 14 years old, x-ray films of the skull and right hand

TABLE 1. Laboratory Data.

DATUM	WITH PITUITARY EXTRACT	WITHOUT PITUITARY EXTRACT
Serum		
Calcium (mg /100 cc)	10.6	10.1
Phosphorus (mg /100 cc)	4.6	4.3
Chloride (mg /100 cc)	363	364
Total protein (gm /100 cc)	5.9	6.2
Albumin (gm /100 cc)	4.0	3.9
Globulin (gm /100 cc)	1.9	2.3
Sugar (mg /100 cc)	107	106
Cholesterol (mg /100 cc)	175	
Hematocrit (%).	38	41

months. He had measles, mumps and chicken pox. About 6 months before the onset of the diabetes insipidus, he hurt his head, which raises the question whether the injury had anything to do with the precipitation of the disease; x-ray studies of the skull were negative. At the onset of the disease, the daily fluid intake and output were 3 to 4 liters, and he voided about every 15 minutes. When he was about 8 years old, his mother noted that he was not growing so fast as his twin sister, and as time went on, this difference in weight and height became more marked. Like his twin, he did well at school until his second year at high school, when he did poorly; he had to withdraw from school the following year. At the age of 11 years, the daily fluid intake and output without pituitary therapy were about 6 to 7 liters—at present, these are about 9 to 10 liters. Pituitary extract administered intranasally or intramuscularly has always reduced the urine volume to normal. At 18, his physical development was retarded, and he had not matured sexually; he did not have to shave. He had become extremely sarcastic. Six months later, however, the patient showed marked sexual changes and had become considerably calmer. His voice

TABLE 2. Record of Height and Weight of Twins.

AGE	JOHN		JOAN	
	HEIGHT	WEIGHT	HEIGHT	WEIGHT
yr.	in.	lb.	in.	lb.
5			41	38
6	44	39	43	42
7			45	49
8	46	46	48	53
9	47	48	50	57
10	49	51	53½	65
11	49½	52	53½	65
12	51½	56	56	71
13	53½	62	58½	77
14	55	64	61	92
15	57	73	62½	97
16	58	76	63½	102
17	60½	81	64½	106
18	62	85	66	111

and wrist were obtained to determine whether there was any difference in their bony development. The reports were as follows:

Films of John's skull shows a smooth vault, with no localized changes or signs of pressure; no abnormal calcification is seen and the dental development is

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normal. In the film of the right hand and wrist, all the epiphyses are wide open.

Films of Joan's skull show it to be normal; it is 0.8 cm. greater in anteroposterior diameter than that of her twin. There is no appreciable difference in the dental development. A film of the right hand and wrist shows that the epiphyses of the terminal pha-

tip of the finger during that time. In spite of this, his epiphyseal development is delayed. Apparently, Joan got her growth earlier, and her epiphyses matured earlier. John's growth and epiphyseal union have both been delayed.

At the age of 18½ years, x ray films of John showed no change in the cranial vault or in the sella. The mandible



FIGURE 1. Photographs of the Twins.

*The one on the left was taken when they were eight years old; that on the right, when they were fourteen*

langes are closed and the others maturing, in other words, there is a difference of 2 or 3 years in bone age.

At the age of 17 years, the twins were x-rayed again; the reports were as follows:

Re-examination of John's skull shows a smooth vault, with no localized changes and no general signs of pressure; the sella turcica remains normal. Re-examination of the right hand and wrist shows all epiphyses open, with not even the changes of maturation (Fig. 2). The findings indicate a definite delay in epiphyseal union.

Re-examination of Joan's skull shows the sella to be normal, with no signs of intracranial pressure and no localized lesions. Re-examination of the right hand and wrist shows all epiphyses closed (Fig. 2); the bones appear normally developed.

Comparing the films of the twins at the age of 14 years and those at the age of 17 years, there has been no appreciable growth of the skull in either case. Comparing the hands, there has been no growth of Joan's bones, but John's have definitely grown, being 1 cm. longer from the base of the third metacarpal to the

appeared slightly larger and heavier, and the second molars had erupted since the examination 18 months previously. The right hand and wrist showed only slight changes, indicating beginning maturation of the epiphyses, particularly at the proximal end of the proximal phalanx of the middle finger. All the epiphyses were still open, and growth had not yet ceased.

All the films were interpreted by Dr. M. C. Sosman.

### Discussion

These twins are of interest because one twin developed diabetes insipidus at the age of five and a half years and subsequently had a retarded growth and development. In contrast, the other twin grew and matured normally. The x-ray findings are of interest because the twin with diabetes insipidus had a smaller skull than his twin sister and also because all the epiphyses of the right hand and wrist were open at the age of eighteen and a half years, whereas his twin sister's epiph-

yses were closed at seventeen years. The findings indicated a definite delay in epiphyseal union in the twin with diabetes insipidus.

Patients with diabetes insipidus do not necessarily have a retarded growth and development, although some do. With such a striking differ-

betes insipidus occurred among them. In none of these cases were there twins.

#### SUMMARY

This report presents a study of a pair of eighteen-year-old nonidentical twins, one of whom

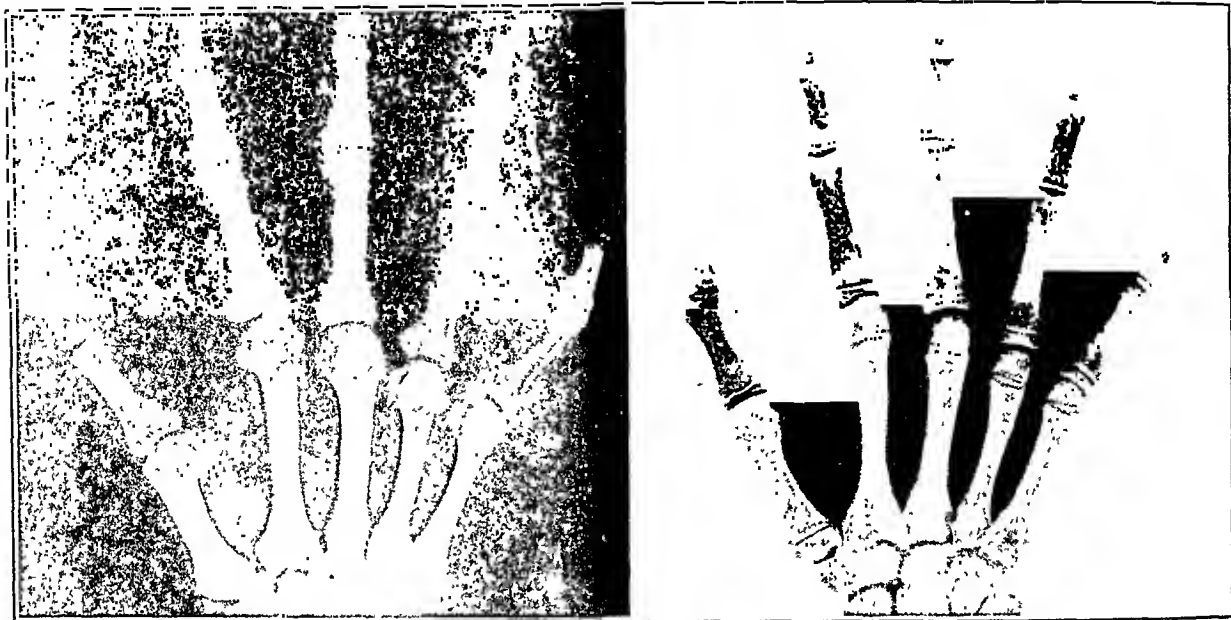


FIGURE 2. X-ray Films of the Right Hand of Each Twin at the Age of Seventeen Years.

*At the left, the film of the normal twin's hand is shown; at the right, that of the twin with diabetes insipidus, in which the epiphyses are open.*

ence in the progress of growth of these twins, it appears that a disturbance in the anterior pituitary gland of the twin with diabetes insipidus interfered with his growth and bony development.

In the literature, I have been unable to find any reference to the occurrence of diabetes insipidus in one or both twins. Weil<sup>1</sup> and his son<sup>2</sup> discussed the inherited tendencies or the familial characteristics of diabetes insipidus. They described in detail the 220 members of five generations of one family, headed by a man with diabetes insipidus, and reported that 35 cases of dia-

developed diabetes insipidus at the age of five and a half years. The twin with diabetes insipidus had retarded growth and development. The normal twin grew and matured normally.

The x-ray findings of the right hand and wrist were interesting because there was a definite delay in the epiphyseal union in the twin with diabetes insipidus.

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## MEDICAL PROGRESS

### INDUSTRIAL HYGIENE

SHERMAN S. PINTO, MD,\* AND MANFRED BOWDITCH†

BOSTON

ANY branch of medicine may be broadened along two main lines: through an increase in scientific knowledge, such as discoveries in individual laboratories or clinics, and through widespread application of new discoveries, that is, through popularization. Both lines are of definite importance, since only the widespread application of new discoveries can justify the great expenditures of time and money necessary to research.

Industrial hygiene is concerned with the preservation and improvement of the health of workers. In this field, many significant advances have been made in the last few years, but not until very recently has any emphasis been placed on the application of these advances to as large a proportion of the industrial population as possible. Before 1936, there were only half a dozen state departments conducting industrial-hygiene activities in even a limited way.<sup>1</sup> Under the stimulus of funds supplied wholly or in part by the federal government, thirty two states and four cities now support industrial hygiene units,<sup>2</sup> and these states have a working population of forty million people. Thus, the mechanism is being rapidly perfected for bringing about widespread application of the knowledge of industrial hygiene.

It is through the general practitioner that the new discoveries of industrial hygiene must be brought to the worker, for only 15 per cent of workers in this country have the advantage of full time medical services during working hours.<sup>3</sup> Industrial absenteeism due to injury and sickness can be greatly influenced by the skill with which the private practitioner handles these cases,<sup>4</sup> and on him rests the responsibility for recognizing early, and treating correctly, disorders caused by industrial operations and environment. He must also have the preventive side of the picture in mind and must seek to determine whether measures may be taken to reduce the frequency of the illnesses being treated. It has been said that any community may decide for itself whether or not it wishes to suffer from diphtheria. Just as truly may it be said that any industry may decide

whether or not health is to be threatened by employment in its plants.

Both state and federal industrial-hygiene units are set up to study problems and furnish advice along medical, chemical and engineering lines. In addition, most state medical societies have a committee on industrial health or the equivalent. It is to agencies such as these that the private practitioner should turn when new problems in the field of industrial hygiene arise.

#### DERMATITIS

Skin irritation from substances used in industry present numerically the greatest number of industrially induced cases of disease. As industry develops, so do new methods and chemicals that frequently cause skin irritation, even though the more serious toxic manifestations are not found. Sterner<sup>5</sup> states that, in one company alone, from 10,000 to 12,000 different chemicals are employed, and that between one and several hundred employees may be exposed to any of them.

Among the commoner causes of dermatitis in industry are the cutting oils. These oils apparently cause dermatitis by blocking the sebaceous glands.<sup>6</sup> Because of this mechanical blocking, the natural oily secretions of the skin are held back, accumulate, harden, and eventually cause enough irritation to produce a dermatitis. Infection also plays a part, but is believed to be produced by organisms normally present on the skin.<sup>7</sup> For cleansing the oil from the skin, a mixture of pure liquid soap and sawdust in equal parts has been recommended. Klauer et al.<sup>8</sup> have suggested the use of a mixture containing 45 per cent each of sulfonated neat's foot oil and light liquid petrolatum and 10 per cent of a 25 per cent aqueous solution of gelatin. To one part by weight of the oil mixture are added one and a half parts of white granulated corn meal. Chlorobutanol (0.5 per cent) may be added to prevent mold or bacterial growth. This mixture of corn meal oil replaces harsh abrasive soaps and brushes or rags in the daily cleansing of the skin. Klauer's article contains valuable formulas for other skin-cleansing detergents and skin protective creams that may be satisfactorily used in numerous industrial conditions.

All articles in this series will be published in book form the current volume is *Medical Progress Annual, 1940* (Springfield Illinois: Charles C. Thomas & Company, 1941, \$4.00).

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Other industrial causes of dermatitis are too numerous to list, but attention should be called to the chlorinated naphthalenes, chlorinated hydrocarbons<sup>9</sup> and the general class of substances known as resins.<sup>10</sup> The use of these materials is increasing, but an accurate diagnosis can be made only by careful search into the occupational history of the patient.

From the wide variety of industrial substances known to cause dermatitis, it is apparent that they may act in several ways. The dermatitis may result from primary irritation or mechanical action, or may be an allergic response. At one time, it was thought that hypersensitive persons could be determined by pre-employment patch testing. Experience has shown this method to be impractical, since a large proportion of industrial allergic sensitivity is acquired only after employment and contact with the offending substance for weeks or months.

An infectious disease of occupational origin that first manifests itself by the appearance of a typical skin lesion is anthrax. The incidence of this condition is increasing, and fatal results can be prevented only by early diagnosis and treatment. The use of serum is still the method of choice for combating infection and toxemia.<sup>11</sup>

#### BENZOL

Because of its physical and chemical characteristics, benzol is one of the best solvents from the industrial point of view. From the standpoint of health, however, it is one of the most dangerous to use, since it is likely to cause disorders of the blood-forming organs. Recent studies by several investigators have done much to show how protean are the early manifestations of the action of small amounts of benzol on the body. Most industrial workers inhale the fumes of benzol, and are chronically poisoned by this method, rather than through skin absorption. Evidence of benzol exposure and absorption may be found by a change of the inorganic-total sulfate ratio of the urine.<sup>12, 13</sup> Bowditch and Elkins,<sup>14</sup> in studying this ratio among workers exposed to benzol, found that it was lowered after exposure to benzol vapors. Although this test alone does not indicate benzol poisoning, it is a good measure of the amount of benzol absorption following exposure.

The initial blood changes in benzol poisoning are of the utmost significance, since it is only by early detection of this condition that extensive damage can be prevented. Hunter<sup>15</sup> found many types of blood changes resulting from benzol—polycythemia, anemia, leukocytosis, leukopenia,

leukemoid blood conditions, eosinophilia, megalocytosis and microcytosis. He states that the early diagnosis of poisoning depends on an evaluation of the complete blood picture rather than on the existence of a leukopenia. Erf and Rhoads<sup>16</sup> studied the blood picture in early benzol poisoning and also found an extremely varied, but abnormal, blood picture. They noted anemia, leukopenia, thrombocytopenia and elevation of reticulocyte counts as commonly occurring changes. Greenburg et al.,<sup>17</sup> in a study of 332 workers exposed to benzol, found the following significant abnormalities: an anemia; an increase in the mean corpuscular volume of the red cells; and a reduction in blood platelets. These workers state that too great reliance should not be placed on the leukocyte count *alone* as a rapid means of detecting cases of benzene poisoning. In their experience, leukopenia was found more frequently in severe than in early cases.

Goldwater<sup>18</sup> decided from studying a large group of patients exposed to benzol vapors that the abnormalities most frequently observed were anemia, macrocytosis and thrombocytopenia. In a later study of recovery from chronic, mild benzol poisoning, he<sup>19</sup> found that damage to the blood-forming organs may persist for at least two years following cessation of exposure, although the majority of people recover within fourteen months.

From these and other studies, authorities have attempted to set a safe limit for the amount of benzol that may be in the air breathed by workmen. One group<sup>20</sup> has suggested 75 parts per million as a safe and attainable figure, whereas another observer<sup>15</sup> rather pessimistically says, "It is doubtful whether any concentration of benzene greater than zero is safe over a long period of time."

With these new methods for diagnosing benzol poisoning available, it is incumbent on all physicians treating workers who might possibly be exposed to benzol vapors to study such patients from this point of view. If the old-time concept of leukopenia is thought of as the sole diagnostic sign of benzol poisoning, most of the chronic, and sometimes fatal, cases of benzol poisoning will be overlooked.

#### CARBON DISULFIDE

Hamilton,<sup>21</sup> in reviewing carbon disulfide poisoning, points out that diagnosis is difficult, since so many of the symptoms are subjective. The mental symptoms, which are most striking, range from simple irritability and depression to manic-depressive insanity. Other symptoms are neuritis,

ocular manifestations,—such as enlargement of the blind spot and diminution of the corneal reflex,—dermatitis and gastrointestinal disturbances. From the laboratory side of the picture, diagnosis may be made more certain by analyzing biologic fluids for their carbon disulfide content according to the method of McKee.<sup>22</sup> Since this falls rapidly after exposure ceases, analyses must be made during or shortly after the period of exposure.

### LEAD

Progress in the diagnosis of lead poisoning has been made primarily in the laboratory. More sensitive methods for the analysis of urine and blood are a great aid in confirming or refuting a tentative diagnosis of lead poisoning. The most important advances in technic have been made by Willoughby and Wilkins,<sup>23</sup> Ross and Lucas<sup>24</sup> and Kehoe et al.<sup>25</sup> Parenthetically, it may be stated that the accurate determination of lead in blood and urine is one to be undertaken only by a skilled chemist. A number of state occupational hygiene agencies are capable of making these tests, and the practitioner will do well to get in touch with such units when he desires to have the tests made.

### MERCURY

One of the recent bright spots in the prevention of disease concerns the use of mercury in the fur felt hat industry. 'Mad as a hatter' is a phrase that has long been a byword in the English language; translated into terms of industrial medicine, it means simply an occupational mercury poisoning such as the felt hat maker has frequently acquired. Mercury is used for 'carrotting' fur, a process by which fur is so changed that it may be made into felt. Through the combined efforts of industrialists, laborers, physicians and governmental agencies, it was decided that only nonmercury-carroted fur could be used for felt hat making in the United States after December 1, 1941.<sup>26, 27</sup> This splendid step forward, possible only through the co-operation of all interested groups, is an example of how such problems might well be attacked. When the prevalence of mercury poisoning in the fur felt hat industry was recognized, an effort was made to find substitutes for the process in which mercury was used. After such substitutes had been found, industry willingly co-operated to replace the highly dangerous process with a far safer one.<sup>28</sup>

### CONCENTRATION OF CHEMICALS IN AIR

To clarify the question of air concentrations of toxic substances that are considered comparable with safe working conditions, Table I is given.

In it, the air concentration of the industrial substance is expressed as parts per million (ppm) unless otherwise specified. This list is abstracted.

TABLE I Suggested Maximum Safe Concentration of Certain Industrial Chemicals

GAS OR VAPOR	CONCENTRATION ppm	GAS OR VAPOR	CONCENTRATION ppm
Ammonia	100	Lead	0.15*
Amyl acetate	400	Mercury	0.10*
Acetone	1	Methanol	200
Benzene (benzol)	75	Nitrobenzene	5
Carbon disulfide	15	Nitrogen oxides	10
Carbon monoxide	100	Ozone	1
Carbon tetrachloride	100	Phosgene	1
Chlorosulphatene	1 to 5*	Phosphine	2
Ether	400	Sulfur dioxide	10
Formaldehyde	20	Tetrachlorethane	10
Gasoline	1000	Toluene	200
Hydrogen cyanide	20	Trichlorethylene	200
Hydrogen sulfide	20	Zinc oxide	15*

\*Milli grams per cubic meter

from that recently published by a group conversant with this problem.<sup>29</sup>

### THE FUTURE

Each new chemical introduced to industry is a potential health hazard until proved otherwise. Under the present stimulus of national defense, the use of certain materials has increased tremendously. Although most of these are chemicals with which the practitioner is more or less familiar, the industry of war utilizes some materials peculiar to itself. The following are mentioned to warn how and where danger may be expected.

Tetryl is an explosive that is notorious for the amount of dermatitis it causes among those handling it. Silver<sup>29</sup> has reviewed the subject thoroughly with reference to workers in England affected during the present war.

Trinitrotoluene (TNT) causes both dermatitis and general systemic disease. The earliest sign of systemic poisoning is a mild cyanosis. Moderate exposure frequently causes anemia, whereas severe poisoning may cause acute yellow atrophy of the liver or an aplastic anemia.<sup>30, 31</sup>

Radium is being used in large amounts to produce luminescent paints. As these paints are applied to such objects as airplane instrument dials, it is readily seen that the quantity used will steadily become larger. Radium poisoning, with resultant bone tumors, is well known, but if radium is handled according to specifications recently issued by the Bureau of Standards, such tragic accidents should not occur.<sup>32</sup>

73 Joy Street

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recorded, so that I assume none were done. No mention is made of the white-centered petechiae that are found in endocarditis of the verrucous type. There are many pathologists who believe that no clear-cut findings are available to differentiate lupus and Libman-Sachs syndromes except greater than average involvement of the endothelium. This is especially true of cardiac valvular disturbance.

Without any evidence for the diagnosis except the statistics that almost 50 per cent of cases of disseminated lupus have coarse verrucous endocarditis, it seems best to ignore this pitfall. My diagnoses, therefore, are disseminated lupus erythematosus, healed tuberculous adenitis and terminal pneumonia. It is possible that the arthritis was rheumatoid in type and that there was an incidental pyelonephritis.

#### CLINICAL DIAGNOSES

Lupus erythematosus disseminatus.  
Arthritis deformans.  
Tuberculosis of lymph nodes.

#### DR. WARTHIN'S DIAGNOSES

Lupus erythematosus disseminatus.  
Tuberculous adenitis, healed.  
Pneumonia, terminal.  
Arthritis, rheumatoid?  
Pyelonephritis?

#### ANATOMICAL DIAGNOSES

Acute disseminated lupus erythematosus.  
Polyserositis, chronic fibrous.  
Bronchopneumonia.  
Generalized lymphadenopathy.  
Tuberculosis of cervical lymph nodes.  
Rheumatoid arthritis of wrist and phalanges?

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This is one of the cases that discourage the morphologist. The immediate

cause of death was, of course, a terminal bronchopneumonia, but of the fundamental underlying disease there was extremely little visual evidence. The skin rash was still present but was naturally much less vivid than it had been during life. Slight fibrous adhesions were found in both pleural cavities, in the pericardium and between the diaphragm and the upper surface of the liver, to indicate that the patient had had at one time a polyserositis. There was no endocarditis, and all the visceral organs except the lungs were entirely normal. A few old calcified lymph nodes were found in the lower cervical region, but there was no evidence of active tuberculosis. One evidence of probable activity besides the skin rash was the finding of a generalized lymph adenopathy. The retroperitoneal lymph nodes, for instance, were more or less uniformly about 1 cm. in diameter, pink, soft and edematous.

Microscopic examination gave us little more information. The lymph nodes did show congestion and necrosis of the germinal centers, a very constant finding in acute disseminated lupus. A few lymphocytes were found in the pericardium and pleura. The cervical lymph nodes showed completely inactive tuberculosis. Even the kidneys proved entirely normal — not only were there no wire-loop lesions, but even focal glomerulonephritis, which in our experience is frequent in this disease, was lacking. The most important function of the pathologist in such a case is to rule out other disease entities. That we could easily do, and hence there can be no doubt that Dr. Warthin's diagnosis of acute disseminated lupus was correct. It is quite unusual in lupus to see permanent changes in the involved joints. Unfortunately, we did not have permission to examine the joints of the hands in this patient, and we therefore cannot rule out the possibility of a complicating rheumatoid arthritis.



ocular manifestations,—such as enlargement of the blind spot and diminution of the corneal reflex,—dermatitis and gastrointestinal disturbances. From the laboratory side of the picture, diagnosis may be made more certain by analyzing biologic fluids for their carbon disulfide content according to the method of McKee.<sup>22</sup> Since this falls rapidly after exposure ceases, analyses must be made during or shortly after the period of exposure.

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Arnine .....	1	Methanol .....	200
Benzene (benzol) .....	75	Nitrobenzene .....	5
Carbon disulfide .....	15	Nitrogen oxides .....	10
Carbon monoxide .....	100	Ozone .....	1
Carbon tetrachloride .....	100	Phosgene .....	1
Chloronaphthalene .....	1 to 5*	Phosphine .....	2
Ether .....	400	Sulfur dioxide .....	10
Formaldehyde .....	20	Tetrachlorethane .....	10
Gasoline .....	1000	Toluene .....	200
Hydrogen cyanide .....	20	Trichlorethylene .....	200
Hydrogen sulfide .....	20	Zinc oxide .....	15*

\*Milligrams per cubic meter.

from that recently published by a group conversant with this problem.<sup>20</sup>

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# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

## CASE 27501

### PRESENTATION OF CASE

A thirty-six-year-old factory worker was admitted to the hospital because of pain in the right shoulder.

He was well until the insidious onset of intermittent dull aching pain in the right shoulder, about six months before entry. After two months, he was aware of swelling of the shoulder and limitation of motion upward and backward. The pain gradually increased in intensity, became constant, and radiated to the tips of the fingers of the right hand. In the few weeks preceding entry, the pain was so severe that the patient was scarcely able to sleep. There was a loss of 6 pounds in weight. A physician, consulted early during the illness, told the patient that he had "rheumatism." Four days before entry, this physician took a roentgenogram of the shoulder and, on the basis of the film, referred the patient to the hospital.

The patient's mother had died of carcinoma of the stomach. There was no other family history of cancer. The patient had always been in good health, except for a railway accident twenty-six years before entry in which part of his left leg was avulsed, necessitating skin-graft treatment.

On admission, the patient appeared thin, with obvious swelling of the upper right arm and shoulder. This swelling consisted of a peach-sized mass, apparently situated deeply between the neck of the humerus, the acromion and the distal end of the clavicle. A stony-hard small mass and a soft small mass, both freely movable, were palpable in the position of lymph nodes of the right axilla. The arm was held in 40° abduction, at rest, and could be abducted to only 90°. External and internal rotation were likewise limited, and the arm could not be placed behind the back. The chest was clear, and physical examination was otherwise negative, except for signs of old injury to the left lower leg, which was bowed anteriorly and covered by tense, scaling, atrophic skin.

The temperature, pulse and respirations were normal. The blood pressure was 138 systolic, 80 diastolic.

Examination of the blood showed a white-cell count of 11,100 and 95 per cent hemoglobin. The blood calcium was 11.3 mg. and the phosphorus 3.4 mg. per 100 cc., and the phosphatase was 16.3 Bodansky units. The urine was normal.

A roentgenogram of the right shoulder showed destruction within the upper end of the shaft of the humerus, with extensive condensation of the bone and some new-bone formation. Discrete areas of calcification were evident, high in the axilla. Roentgenograms of the chest and abdomen were negative.

On the fifth hospital day, an operation was performed.

### DIFFERENTIAL DIAGNOSIS

DR. CLIFFORD C. FRANSEEN: This history could fit in with a number of lesions, and we shall have to rely heavily on the x-ray findings for our diagnosis.

DR. JAMES R. LINGLEY: The films show this extensive lesion involving the proximal extremity of the humerus, characterized by bone destruction and a large amount of new-bone formation. The new bone extends out into the soft tissue for a considerable distance, and there are separate discrete areas of calcification high up in the axilla. The chest shows no evidence of disease.

DR. FRANSEEN: I was inclined, before I saw the x-ray films, to discount the small calcified mass in the axilla, which was described as small and stony hard, as incidental, but a view of the films suggests that the mass is definitely related to the lesion in the shoulder. It is not infrequent in cancer of the breast to see calcified lymph nodes in the axilla or supraclavicular region, which often make it difficult to decide whether metastases are present. Sometimes, for example, the presence of calcified supraclavicular lymph nodes may mislead one in deciding whether a radical mastectomy should be done.

I see no alternative but to go through the usual routine of differential diagnosis. When it is difficult to make a diagnosis, it is customary to deplore the lack of further information. The blood serologic findings in this case are not reported. Before seeing the films, I had syphilis in mind, perhaps because I was sensitized to the diagnosis by a recent case in a man of this age who also had involvement of the upper end of the humerus. There is obviously a large soft-tissue mass suggestive of tumor, and although syphilis can simulate any lesion of bone, certainly there is nothing about this case that, on first glance, suggests syphilis to me. The blood chemical f

a little puzzling, and I wonder if they had any relation to this lesion. There is a good deal of calcification for some reason, and it may have been that that amount of calcification or mobilization of calcium was responsible for the slightly elevated blood calcium. In Aub's<sup>1</sup> series of calcium determinations, the average normal was 10.8 per 100 cc. (Fiske method), and in only 3 cases, among several hundred examined, it ranged from 11.0 to 11.3 mg. It is difficult to know why it should be so high in this case. Of course in the last

We have already ruled out syphilis, but the elevated phosphatase reminded me that we had one patient with an elevated phosphatase apparently caused by antisyphilitic treatment. When patients receive Coley's toxins for tumors of the bone, toxic hepatitis, in addition to some elevation of the phosphatase, results. If the patient had received either of these treatments, it could possibly be the explanation here.

The picture does not look at all characteristic of osteomyelitis to me, with so much new-bone



FIGURE 1. *Sclerosing Osteogenic Sarcoma of the Head of the Humerus, with Two of the Ossified Lymph-Node Metastases.*

two or three years, a good many cases of various bone lesions have been reported with elevated calcium. Multiple myeloma is particularly notorious in this respect, but in most of these cases the phosphorus is more nearly normal. Consequently, on the basis of these blood chemical findings alone, I do not believe that we can make any flat-footed statement. The phosphatase of 16.3 Bodansky units, of course, is elevated, perhaps to four times normal, and with the amount of new-bone formation here, this value is perfectly compatible with the observations in the x-ray study concerning the presence of ossification.

Tuberculosis always comes to mind. My experience with tuberculosis is rather limited. The patient was rather old, since tuberculosis is usually a juvenile disease. It can occur in this location, but there is a large soft-tissue tumor mass in conjunction with the lesion. I do not consider tuberculosis very seriously for these reasons.

formation in this region. Obviously, there is a large mass, which does not seem to be inflammatory.

Granulomas of bone do not have to be considered seriously. They are almost purely destructive, and so far as I know, the end of a long bone is an unusual site for them.

Hyperparathyroidism is suggested only because of the blood chemical findings, but certainly the x-ray picture does not suggest anything I am familiar with in this disease.

Lymphoma has been reported to simulate various types of bone tumors, sometimes with considerable production of new bone. There is nothing else about the patient to suggest the diagnosis. He lost 6 pounds in weight, and there are other things suggesting that there might have been some underlying systemic condition, but certainly it was not characteristic of the usual picture of lymphoma of bone, which more commonly occurs

in the late stages when it is evident elsewhere in the body.

Ewing's tumor could occur in this man. He was at the upper limits, perhaps, of the age when it is most common, and there was an unusual amount of new-bone formation. The lesion was near the head of the bone, which is a less likely site.

The presence of so much calcification in the tissues, and even in the lymph nodes, presumably, disturbs me a good deal. I know of no case of osteogenic sarcoma in which there has been calcification in the regional nodes themselves. Calcification occurs in the lungs in metastases from osteogenic sarcoma, and I have done phosphatase determinations on the tissues in these nodules and found them as high as that in the original tumor. I remember a case at the Palmer Memorial Hospital in which the lymph nodes suggested disease in the x-ray picture, but at the time of operation these nodes were removed and showed no calcification by pathological examination.

I have never seen any metastatic lesions that had laid down so much new bone, and the man is also relatively young. There is nothing about the picture to suggest Paget's disease. The other thing one would have to think of with so much calcification around the joint is a Charcot joint or, possibly, the condition that resembles it on x-ray examination and is secondary to syringomyelia. There is no suggestion here of such disorganization of the structures of the bone. We have no serologic evidence of syphilis, so far as Charcot's joint goes, but the lesion could occur without it from syringomyelia.

I am left with nothing but low grade osteogenic sarcoma to consider. I have seen cases of osteogenic sarcoma with a good deal of calcification in the surrounding tissues. I am at a loss to explain the case on any other basis with the evidence at hand. A conclusive diagnosis would depend on the results of the biopsy examination.

DR. LINGLEY. The roentgen appearance of the lesion in the humerus is typical of osteogenic sarcoma. The case is very interesting to me because I have never seen calcified osteogenic-sarcoma metastases in lymph nodes. I have seen them in the lungs, but not in the regional lymph nodes. It appears that such a metastasis occurred in this case.

DR. GRANTLEY W. TAYLOR. We were very much interested in this problem in the Tumor Clinic, and we believed that we should confirm the diagnosis by biopsy of one of the nodes before proceeding to therapy. We were able to confirm

the diagnosis of osteogenic sarcoma from one of the lymph nodes. The case is uniquely interesting because lymph node metastases from osteogenic sarcoma are very rare. In any event, Dr. Shields Warren,<sup>2</sup> when he reported metastases from various types of sarcomas in his series, had only one case of lymph node metastasis from osteogenic sarcoma. There are a few others. Dr. Thomas J. Anglem had a case similar to this in which actual bone formation was taking place in the regional lymph nodes; but such cases must be extremely rare, since both lymph node involvement and calcification are rather unusual in metastases of osteogenic sarcoma. Ossifying metastasis even in the lungs is rare enough to excite comment, and here we have the two unusual features combined in one case.

DR. FRANSEEN. I went over all the bone tumors at the Radiumhemmet in Sweden to see if I could find any case with metastases to the nodes, but I could not find one case.

#### CLINICAL DIAGNOSIS

Osteogenic sarcoma of humerus, with metastases to axillary lymph nodes.

#### DR. FRANSEEN'S DIAGNOSIS

Osteogenic sarcoma of humerus

#### ANATOMICAL DIAGNOSIS

Osteogenic sarcoma of humerus, with ossifying metastases in the regional nodes.

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY. I presented this case before the American College of Surgeons when Dr. Murray Copeland was present, and he said he had seen a number of cases of osteogenic sarcoma with metastases to nodes; in fact, he put the figure as high as 5 to 7 per cent, which was ever so much higher than I should have supposed. I suspect that the figures were probably compiled from autopsy material rather than from clinical examination.

This patient had a number of calcified nodes in the axilla that showed extensive ossification. The primary tumor was a very characteristic osteogenic sarcoma arising in all probability in the diaphysis just next to the epiphyseal line, but it had crossed it and invaded the head extensively. Microscopically, it is a relatively slowly growing, sclerosing tumor, with marked bone formation. The picture in the lymph nodes is indistinguishable from that in the primary tumor.

DR. TAYLOR. Is there definite evidence that these lymph nodes had been invaded by the disease?

DR. MALLORY: In one, in particular, we could see a central mass of bone completely surrounded by lymphoid tissue.

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#### CASE 27502

##### PRESENTATION OF CASE

A twenty-six-year-old single woman entered the hospital complaining of a rash on the skin.

Seven weeks before entry, the patient developed a chill and some fever. She continued to have fever and at least one chill each day for the following week. During the second week of her illness, the chills were less frequent, but the fever persisted. Five weeks before entry, a red spot appeared on the right cheek. This continued gradually to spread over both cheeks, nose, neck, upper part of chest, arms and finally to the legs. The patient soon noticed that her fingers were also very red and sore. Three weeks before admission, she began to have a considerable amount of putrid, often blood-stained discharge from her nose. During this period, she went downhill steadily, slept poorly, and had a very poor appetite.

Her father had died of influenzal pneumonia at the age of thirty-nine. Her mother, two brothers and one sister were living and well. There was no history of any chronic disease in the family.

Ten years before entry, the patient was admitted to this hospital for enlarged cervical lymph nodes. A biopsy was done, and a diagnosis of tuberculous adenitis was made. After leaving the hospital, she went to a sanatorium, where she gained 52 pounds in thirteen months. She remained at home for about a year and a half and then returned to the sanatorium because her hands had begun to swell and had become painful. She was finally discharged after three years and was well at home for about two years. During this period, her hands became deformed.

Physical examination showed a poorly developed and very poorly nourished woman, lying quietly in bed, who appeared acutely ill. The skin over the nose and cheeks was very red and slightly indurated. Smaller bright-red, smooth areas were found on the neck and upper part of the sternum. There were similar lesions, about 5 cm. in extent, on the upper part of the back at about the seventh to ninth dorsal spines. The skin of the arms, particularly the extensor surfaces, had many of these flat, red, slightly indurated lesions, which had coalesced, giving an almost complete involve-

ment of the skin. The fingertips were red, tender and in some places cracked open. The legs had more widely scattered lesions. There were a few excoriations over the abdomen. The mucous membrane of the mouth and nose showed a few scattered hemorrhagic spots. The breath was very foul. There was a foul-smelling, abundant, mucopurulent hemorrhagic discharge from the nose. The teeth were in fair condition. The gums were dark red and hemorrhagic. All the cervical, axillary and inguinal lymph nodes were enlarged, some up to 1 or 2 cm. in diameter; they were hard and slightly tender. Both hands were deformed by an arthritic process and could not be opened or closed; the phalangeal joints were enlarged.

The temperature was 102.1°F., the pulse 116, and the respirations 26.

Examination of the urine showed a specific gravity of 1.008 and a sediment containing 10 to 12 white blood cells in small clumps, many cellular and granular casts and numerous bacilli per high-power field. Examination of the blood showed a red-cell count of 3,720,000 with a hemoglobin of 70 per cent, and a white-cell count of 3900 with 70 per cent polymorphonuclears. A blood Hinton reaction was negative. The bleeding time was 3½ minutes. The nonprotein nitrogen was 21 mg., the cholesterol 83 mg. and the serum protein 7.7 gm. per 100 cc.

A chest film showed marked calcification of all the lymph nodes in the neck. This calcification lay over both apices, so that it was difficult to decide whether the process was in the lung fields. There was no beading or mottling suggestive of tuberculous activity.

The temperature ranged between 99 and 102°F. The joint pains were quite severe, and the patient was given 75 gr. of sodium salicylate daily. She developed edema of the face and complained of a sore throat. Salicylates were stopped because of marked vomiting. On the thirteenth day, she became comatose, and rales were heard in the chest. She had more bleeding from the mouth and died that day.

#### DIFFERENTIAL DIAGNOSIS

DR. THOMAS A. WARTHIN: Certainly, the acute onset of septic constitutional symptoms, followed by the appearance of a widely disseminated bright-red rash, narrows the differential diagnosis to a small group of disturbances. Typhoid fever can be dismissed immediately because of the character of the skin lesions. So also can the septicemia group, including subacute bacterial endocarditis, meningococcemia, and staphylococcal, colon bacillus and streptococcal infections. Erythema multi-

forme, associated perhaps with severe acute rheumatic fever, would undoubtedly have exhibited a number of typical vesicular lesions of the iris. Undulant fever, when associated with skin manifestations, presents a more discrete papular eruption. The rickettsial diseases are of shorter duration than the infection in this case, and their petechial and hemorrhagic rashes do not coalesce so strikingly. I know of no fungous infection associated with skin eruptions in which papular or pustular lesions do not predominate. The negative blood Hinton reaction completes rejection of syphilis as a possibility.

When the patient was sixteen, cervical tuberculous adenitis was proved by biopsy, and the patient was apparently successfully treated for over a year at a sanatorium. However, she did return one and a half years later for treatment of painful swelling of her hands, and remained in the institution for three years. During this time, her hands became deformed. Bilateral deforming involvement of the hands due to tuberculous dactylitis appears mainly in infants. Sarcoid does not fit into the picture of the terminal illness and in addition, that diagnosis would force us to conclude that the lymph node biopsy had been incorrectly interpreted. We are told that this deformity was due to an arthritic process, which makes scleroderma unlikely. Furthermore the patient was in a younger age group than most patients with scleroderma, and no mention is made of associated Rynaud's phenomena.

Could military tuberculosis and tuberculosis cutis explain the final illness? I believe not since there is no evidence of military tuberculosis in the chest film. In addition, lupus vulgaris sclerosis erythematosus, which closely simulates lupus erythematosus, is accompanied by marked rather than slightly indurated skin lesions. This results in considerable scarring in the center of the lesions which this case lacked. Ulceration is very prone to occur in tuberculosis cutis of this type.

For final consideration, we have the group of closely related diseases with vascular disturbances, namely, disseminated lupus erythematosus, Libman-Sachs syndrome and periarteritis nodosa. Scleroderma and dermatomyositis also have more or less generalized vascular lesions, but they clinically present quite different pictures, atrophy of the skin and swelling of the muscles predominating, respectively. Periarteritis nodosa commonly affects males, and the presenting symptomatology is apt to be related to the renal, abdominal, neuro-muscular, cardiac or bronchial systems rather than to the skin. Cutaneous lesions of many types besides nodules along superficial arteries have

been described. Leukocytosis, with or without eosinophilia, rather than leukopenia, characteristically occurs in periarteritis.

If one lists the characteristics of this case, one is immediately struck by consistent similarities with disseminated lupus. The patient was a woman, and was in the second to fourth decades of life. She suffered from the frequently present tuberculous adenitis, which has clouded the theories of etiology of the disease. The onset of the final illness was fulminating, with the chills and fever that may occur in a severe case. Chills are not characteristic, but may be present, it is possible that a pyelitis immediately preceded the lupus. The rash appeared after the onset, as it frequently does. Unfortunately, we are not told whether exposure to sunlight precipitated or intensified the rash. The rash was typical in that it first appeared on the face, with gradual spread to the neck, chest, arms and, finally, the legs. It was characteristically bright red and slightly indurated, with a tendency to coalesce. It involved the fingers, and as frequently occurs, the mucous membranes of the hands were involved, but had been so for several years. It is possible that the lesions occurred during an early phase of the disease, in a subacute form that became quiescent, only to flare up acutely seven weeks before the final entry. Such remissions occur frequently in periarteritis nodosa, and less commonly in lupus. Her long stay in the sanatorium stimulates this speculation, and without it one would be forced to add another diagnosis, that of rheumatoid arthritis. As described, the hands could have been rheumatoid, but it is surprising that no other joints were affected. We are told nothing about eyegrounds, blood pressure, lungs or abdomen, and I consequently assume that they were normal, although the involvement of serous surfaces is common. Nausea, vomiting, edema of the face and joint pain are frequently observed.

The laboratory studies revealed the numerous casts so frequently seen in disseminated lupus, and evidence of some bacilluria and pus. These bacilli were probably secondary invaders, although it is possible that a pyelitis precipitated the final illness. However, the kidneys were not severely involved, as indicated by the nonprotein nitrogen level. Usually, there is some azotemia in lupus. The blood count reveals bone marrow depression by the typical anemia and leukopenia. The chest x-ray film helps rule out a military tuberculosis. The final coma, in addition to the rales, is in keeping with terminal lupus. Without mention of heart murmurs, it is difficult to consider the Libman-Sachs syndrome. No blood cultures are

recorded, so that I assume none were done. No mention is made of the white-centered petechiae that are found in endocarditis of the verrucous type. There are many pathologists who believe that no clear-cut findings are available to differentiate lupus and Libman-Sachs syndromes except greater than average involvement of the endothelium. This is especially true of cardiac valvular disturbance.

Without any evidence for the diagnosis except the statistics that almost 50 per cent of cases of disseminated lupus have coarse verrucous endocarditis, it seems best to ignore this pitfall. My diagnoses, therefore, are disseminated lupus erythematosus, healed tuberculous adenitis and terminal pneumonia. It is possible that the arthritis was rheumatoid in type and that there was an incidental pyelonephritis.

#### CLINICAL DIAGNOSES

Lupus erythematosus disseminatus.  
Arthritis deformans.  
Tuberculosis of lymph nodes.

#### DR. WARTHIN'S DIAGNOSES

Lupus erythematosus disseminatus.  
Tuberculous adenitis, healed.  
Pneumonia, terminal.  
Arthritis, rheumatoid?  
Pyelonephritis?

#### ANATOMICAL DIAGNOSES

Acute disseminated lupus erythematosus.  
Polyserositis, chronic fibrous.  
Bronchopneumonia.  
Generalized lymphadenopathy.  
Tuberculosis of cervical lymph nodes.  
Rheumatoid arthritis of wrist and phalanges?

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This is one of the cases that discourage the morphologist. The immediate

cause of death was, of course, a terminal bronchopneumonia, but of the fundamental underlying disease there was extremely little visual evidence. The skin rash was still present but was naturally much less vivid than it had been during life. Slight fibrous adhesions were found in both pleural cavities, in the pericardium and between the diaphragm and the upper surface of the liver, to indicate that the patient had had at one time a polyserositis. There was no endocarditis, and all the visceral organs except the lungs were entirely normal. A few old calcified lymph nodes were found in the lower cervical region, but there was no evidence of active tuberculosis. One evidence of probable activity besides the skin rash was the finding of a generalized lymph adenopathy. The retroperitoneal lymph nodes, for instance, were more or less uniformly about 1 cm. in diameter, pink, soft and edematous.

Microscopic examination gave us little more information. The lymph nodes did show congestion and necrosis of the germinal centers, a very constant finding in acute disseminated lupus. A few lymphocytes were found in the pericardium and pleura. The cervical lymph nodes showed completely inactive tuberculosis. Even the kidneys proved entirely normal—not only were there no wire-loop lesions, but even focal glomerulonephritis, which in our experience is frequent in this disease, was lacking. The most important function of the pathologist in such a case is to rule out other disease entities. That we could easily do, and hence there can be no doubt that Dr. Warthin's diagnosis of acute disseminated lupus was correct. It is quite unusual in lupus to see permanent changes in the involved joints. Unfortunately, we did not have permission to examine the joints of the hands in this patient, and we therefore cannot rule out the possibility of a complicating rheumatoid arthritis.



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## THE RELATION OF THE PRACTICING PHYSICIAN TO INDUSTRIAL MEDICINE

Two articles in this issue of the *Journal* call attention to the important role played by the practicing physician in industrial medicine. As Mr. Bloomfield, of the Division of Industrial Hygiene, United States Public Health Service, points out, the majority of industrial workers are not furnished with medical care by full-time or part-time plant physicians. Furthermore, the chief causes of disability are illnesses arising from nonindustrial diseases, which, in many cases, result from poor living conditions, improper diets and contagious diseases among the workers' families.

Because of the tremendous increase in industrial activity demanded by the defense program and because of the accompanying hazards occasioned

by the speeding-up of production and by the introduction of new methods, the demands for highly trained industrial physicians are much greater than they were several years ago, in spite of the fact that, during the last decade, there has been a gradually widening appreciation of the value of the application of the modern principles of industrial medicine, both to the worker and to the employer. As previously stated, however, the practicing physician is still chiefly concerned with the health of the employee, and it is on him that a great part of the success of the defense effort depends. He should be thoroughly familiar with the details of proper first-aid care, he should be cognizant of symptoms and signs of the commoner industrial intoxicants, he should not fail to consult with his state authorities concerning definite or doubtful cases of industrial disease, and he should give advice regarding improvement of living conditions and diet to the workers and their families. All in all, his responsibility is great and should not be shirked.

## BRUCELLOSIS AND PASTEURIZATION OF MILK

INVESTIGATORS of the problem of undulant fever or brucellosis claim that in various sections of the United States from 5 to 10 per cent of healthy adults give evidence—by positive agglutination or intradermal tests—of having been infected with *Brucella abortus* at one time or another. Dustin and Weyler<sup>1</sup> go so far as to claim that among 4000 patients seen in private practice in Providence, Rhode Island, about 10 per cent gave what they considered sufficient clinical and laboratory evidence to warrant a diagnosis of chronic brucellosis. Such data are difficult to correlate with the figures of the Bacteriological Laboratory, Massachusetts Department of Public Health,<sup>2</sup> which for 1940 show that only about 4 per cent of the serums from cases of suspected brucellosis gave positive agglutination reactions, and those of the Bacteriological Laboratory, Boston City Hospital,<sup>3</sup> which in the last two years list only one positive reaction among serums from approximately 400 cases of unexplained fever on admission. It seems

logical to conclude that either one or the other group of tests is at fault, or that the incidence of brucellosis in Massachusetts is exceptionally low. As a matter of fact, both factors probably play a role.

The so-called "slide technic" has been, and still is, the generally accepted method of testing serums for agglutinating antibodies against *Br. abortus*. The preparations are examined under the microscope, and spontaneous or nonspecific agglutination is apt to be interpreted as being due to the presence of antibodies. On the other hand, the laboratories of the Massachusetts Department of Public Health and the Boston City Hospital have adopted the so-called "tube technic," in which a living or killed suspension of organisms is added to tubes containing various dilutions of serum, and the results are read macroscopically or with a hand lens. Although the latter method is possibly somewhat less sensitive than the former, positive tests are significant—a fact that explains, at least to some extent, the discrepancy between the reported results.

Even if one assumes that agglutinating antibodies are present in 2 to 5 per cent of the serums from healthy adults in other sections of the country, the figures of 4 and 0.25 per cent for cases of suspected brucellosis or unexplained fever, respectively, in Massachusetts are remarkably low, and the only reasonable explanation is the fact that nearly 90 per cent of the milk consumed in Massachusetts is pasteurized. That only 4 of the 52 cases of brucellosis in 1940 occurred in twenty-four contiguous communities in Metropolitan Boston, which contain 40 per cent of the total population of the State and where pasteurization regulations are in effect, and that only 1 case occurred among some 85,000 patients at the Boston City Hospital, are facts that corroborate the evidence given elsewhere in this issue of the *Journal* concerning the effectiveness of pasteurization as a preventive measure against brucellosis.

Such evidence, together with the fact that pasteurization of milk is effective against contamina-

tion by tubercle bacilli, typhoid and paratyphoid bacilli and streptococci, offers a strong argument in favor of the nation-wide adoption of regulations requiring pasteurization. To permit the marketing of raw milk is to subject the inhabitants of any community to needless danger.

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#### MEDICAL EPONYM

##### LITTEN'S SIGN

Professor Moritz Litten (1845-1907), of Berlin, reported "Ueber die normaliter bei jeder Respiration am Thorax sichtbaren Zwerchfellsbewegungen: Eine physiologisch-klinische Beobachtung [On the Movements of the Diaphragm Normally Visible on the Thorax with Each Respiration: A physiologicoclinical observation]" in the *Deutsche medizinische Wochenschrift* (18:273-275, 1892). A portion of the translation follows:

I have observed that it is possible to see the movements of the diaphragm . . . on the thorax in all healthy men. The phenomenon takes the form of a wave motion that, beginning on both sides at the height of the sixth intercostal space, travels downward with maximum inspiration in the form of a straight line or shallow furrow (which makes an acute angle with the ribs) over several intercostal spaces, at times as far as the costal margin. With expiration, it rises again over the same area.

A more detailed account of the phenomenon is given in the paper, "Das Zwerchfellphänomen und seine Bedeutung vom physiologischen und klinischen Standpunkte [The Diaphragm Phenomenon and Its Significance from the Physiological and Clinical Standpoint]," which appeared in the *Verhandlungen des Kongresses für innere Medizin* (13:309-319, 1895). A portion of the translation follows:

The patient to be studied is placed in a horizontal position . . . with his feet toward the window, while the examiner, standing three or four steps away with his back toward the window, observes him from an angle of about forty-five degrees. . . . We are convinced that in a dark room the phenomenon is visible only if a source of light is so placed that the beams strike the thorax from the direction of the feet at an acute angle with the thorax.

R. W. B.

## MASSACHUSETTS MEDICAL SOCIETY

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## FATAL HEMORRHAGE DURING LABOR

A thirty four year old para IX who had had no prenatal care entered the hospital in mild labor.

Physical examination was essentially negative, although the patient was in poor physical condition, anemic and rundown. Palpation of the abdomen revealed a uterus the size of a full term pregnancy.

Five minims of pituitary extract was given and labor progressed slowly but without untoward symptoms until six hours before delivery, when a large clot was passed. From then on, labor was normal; there was still a moderate amount of bleeding, which did not seem to be alarming until the membranes ruptured spontaneously and bleeding became profuse. The baby was delivered normally, and the placenta was expelled forty five minutes later. Between the birth of the baby and the delivery of the placenta, it was estimated that 300 cc of blood was lost. Fifteen minutes after the birth of the placenta, the patient died.

A partial autopsy revealed no intra abdominal hemorrhage and no rupture of the uterus, but a low implantation of the placenta.

*Comment* This death was evidently caused by hemorrhage during labor and after delivery, and the amount of blood lost during labor was undoubtedly underestimated. Autopsy revealed that hemorrhage occurred from the low placenta, whose site had become separated as the lower segment was taken up and the cervix dilated. It is possible that, had this been realized and the membranes ruptured, possibly with the insertion of a bag, the bleeding would have been entirely controlled. The hemorrhage after the birth of the baby cannot be attributed to the low attachment of the placenta and must have been due to relaxation of the uterus. It is barely possible that the placenta separated with the birth of the child, that its separation was not appreciated as soon as it should have been and that the uterus continued to bleed behind a detached placenta.

Since the uterus was not ruptured, it is not fair to suggest that the use of pituitary extract had anything to do with the fatal outcome, however, when this drug is given in the first stage of labor, it should be given in doses of not more than

1 or 2 minims. Transfusion would have helped this patient, but it is evident that the amount of blood lost during labor and after the birth of the baby was not realized.

## DEATH

CRAIGIN—GEORGE A. CRAIGIN, M.D. of Swampscott, died October 24. He was in his seventy ninth year.

Dr. Craigin received his degree from Harvard Medical School in 1890. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

He is survived by his widow and a sister.

## DEFENSE ACTIVITIES

## CIVILIAN DEFENSE

## OFFICE OF CIVILIAN DEFENSE

Dr. George Biehr, chief medical officer of the Office of Civilian Defense, Washington, D. C., has announced the appointment of a subcommittee of the Advisory Board of the Medical Division to prepare recommendations on protective procedures for hospitals in the event of belligerent action. Dr. R. C. Buerki, dean of the Graduate School of Medicine and director of hospitals of the University of Pennsylvania, Philadelphia, a member of the Medical Advisory Board, is chairman of the new subcommittee, and the members are Dr. W. C. Rappleye, commissioner of hospitals, New York City, Dr. A. J. Hockett, superintendent of Tufts Infirmary, New Orleans, Dr. A. J. J. Rourke, medical superintendent of Stanford University Hospitals, San Francisco, Dr. Joseph Turner, director of Mount Sinai Hospital, New York City, and Dr. Huntington Williams, commissioner of health of Baltimore.

The subcommittee held its first meeting at the Hotel Commodore, New York City, on November 8. With Dr. J. M. Mackintosh, former chief medical officer of the Scottish Ministry of Health, as a guest to advise the group measures for preventing or minimizing damage to buildings, handling of casualties, evacuation, provision and protection of supplies, and training of personnel for specific duties in case of bombing were discussed in detail. The basis for discussion was a study made by a committee of the American Hospital Association of physical defense of hospitals, of which Dr. Hockett is chairman. It is expected that a report will be issued jointly by this committee and the subcommittee representing the Office of Civilian Defense.

Dr. Mackintosh also conferred with the staffs of the medical and civilian protection divisions of the Office of Civilian Defense at the Washington headquarters on November 7, he described in detail Britain's organization of its protective services, its early mistakes and the measures taken to correct them. The basic organization for rescue work in a given area consists of three essential groups with a central control, police, rescue and fire services, ARP control and medical service. One of the early mistakes was the belief that it was imperative to have first aid workers on the scene of a bombing immediately. Better experience showed that injured persons were usually buried under the rubble and glass of their homes and that hours of work by the demolition and rescue squads were often necessary before first aid could be given. Dr. Mackintosh emphasized the necessity for a central ambulance control. Ambulances are dispatched only by the central control and are not allowed to move from a bombed

\* A series of selected cases of the members of the section will be published weekly. Comments and questions by subscribers are welcomed and will be discussed by members of the section. Letters will be addressed to Dr. Raymond S. T. T. Secretary, 330 Dartmouth Street, Boston.

area until routes to hospitals have been surveyed. To stop "panic calls" from individuals, private telephones are cut off the moment an air-raid warning sounds. First-aid posts, in addition to their obvious function of caring for the injured, are invaluable as rendezvous for rescue workers, physicians and nurses, as well as the general population, who may become lost in the blackout, frightened, choked and blinded by dust, he said. In the first-aid posts, the workers can clean up, have a cup of tea and return refreshed to their activities.

## CORRESPONDENCE

### MEDICAL OFFICERS WANTED FOR MOUNTAIN REGIMENT

*To the Editor:* On October 30, 1941, the Secretary of War formally announced to the public the formation of the 1st Battalion, 87th Infantry Mountain Regiment (Reinforced), at Fort Lewis, Washington. This is the first unit ever set up in the United States Army for the specific purpose of conducting winter and mountain-warfare training. The War Department has asked the assistance of the National Ski Patrol in securing names of men who wish to volunteer for this unit, and applications from physicians with interest and ability in skiing are particularly wanted. As in all branches of the services, only men physically and professionally qualified will be accepted. Details may be secured by writing to Mr. Charles M. Dole, Chairman, National Ski Patrol, 222 Graybar Building, New York City.

CHARLES C. LUND, M.D.  
Member of Medical Advisory Committee,  
National Ski Patrol

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### DERMATITIS DUE TO RAGWEED

A twenty-five-old farmer was seen at my office on September 22, 1941. Two years previously, he had had an eruption on his face and arms. This was diagnosed as being due to poison ivy. Recently, while haying, he had noticed that each day his legs became very itchy. His job consisted for the most part of standing in the hay and tossing it down into the barn. A week prior to examination, an itchy eruption broke out on his legs.

Examination showed a marked eruption consisting of erythema, papules and vesicles on the back of the neck, the hands and most of the cutaneous surface of the legs. The eruption was most marked at the popliteal spaces and about the ankles. The patient was put on soothing treatment and stopped work, and was promptly relieved. On October 20, he returned to work, avoiding the hay, but doing some odd jobs about the farm. He suffered a prompt recurrence of the dermatitis. He was patch-tested with various contacts, including weeds from the farm, and showed a marked reaction, consisting of erythema, edema and vesicles, to a plant that was identified by the Bureau of Plant Industry as being common ragweed, *Ambrosia artemisiifolia*.

Although most physicians are cognizant of the reactions resulting from contact with poison ivy, oak or sumac, they are apt to forget that other plants may cause a dermatitis.

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## BOOK REVIEWS

*The Minds and Nerves of Soldiers.* By Edward L. Hanes, M.D. 8°, cloth, 221 pp. Pasadena, California: Login Press, 1941. \$3.00.

Dr. Hanes, who served as a member of the Neuropsychiatric Service of the United States Army during World War I, has reviewed his experiences and published his opinions about patients and treatment; the volume is based on an extraordinary number of private documents that he has preserved. Many of the examples given are detailed interviews between the examiner and the recruit. Others are details of the case histories of men, either injured or suffering from psychoneurotic manifestations accompanying warfare. Because this manuscript was apparently written largely at the time the observations were made, there is a freshness about the material not found in the ordinary compilation. The case histories and long notes of interviews, however, are not peculiarly integrated. Because of the author's wide experience, the book has considerable value as a record of neuropsychiatric disease occurring in American soldiers, both in this country and abroad, during World War I. There is no index.

*The Avitaminoses: The chemical, clinical and pathological aspects of the vitamin deficiency diseases.* By Walter H. Eddy, Ph.D., and Gilbert Dalldorf, M.D. Second edition. 8°, cloth, 519 pp., with 28 illustrations and 40 plates. Baltimore: Williams and Wilkins Company, 1941. \$4.50.

As in the first edition of this excellent book, the aim of the authors is to present a small manual on the nature of the various vitamins and their functions considered from the clinical, chemical and pathological points of view. This new edition necessitated the rewriting of most of the text. A feature of work that will undoubtedly attract and profit all readers is the co-ordination and readability of the chapters. The authors make a special effort to identify underlying principles and mechanisms. A considerable number of new illustrations have been added, and the references carefully checked. It is well to quote the opinion of Dr. James Ewing, the eminent pathologist, who writes in the "Foreword," "The preparation of the first comprehensive treatise in English on the pathological responses to vitamin deficiencies emphasizes the importance of the application of morphological control in the study of vitamins."

*A Textbook of Clinical Pathology.* Edited by Roy R. Kracke, M.D., and Francis P. Parker, M.D. Second edition. 8°, cloth, 780 pp., with 223 illustrations, 26 tables and 34 colored plates. Baltimore: Williams and Wilkins Company, 1940. \$6.00.

This is an unusually fine textbook of clinical pathology, the work of experienced teachers in the field, all of whom are teachers in the Middle Western and Southern medical schools. They have succeeded in making it a complete treatise that covers comprehensively, accurately and lucidly every aspect wherein the laboratory may aid in clinical diagnosis. The text is profusely illustrated.

The work is fully up-to-date. Among the many new features are a chapter on the determination of vitamins and hormones and, in the section on clinical chemistry, a description of the methods for determining the sulfonamides in the blood and urine.

(Continued on page viii)

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## HIATUS ESOPHAGEAL HERNIA\*

With Special Reference to a Comparison of Its Symptoms  
with Those of Angina Pectoris

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NEARLY one hundred and seventy years ago, Heberden<sup>1</sup> gave his classic description of angina pectoris. He noted:

The pain is sometimes started in the upper part, sometimes in the middle, sometimes at the bottom of the os sterni, and more often inclined to the left than to the right side. It likewise very frequently extends from the breast to the middle of the left arm. The pain sometimes reaches to the right arm as well as to the left and even down to the hands.

Heberden also mentioned such variations as pain in only one arm and radiation to the jaws or to the epigastrium.

In commenting on the explanation of anginal pain, White<sup>2</sup> states:

Many different conditions can cause pain in the chest even referred to the arms, easily confused with angina pectoris dependent on coronary disease. The gastric and esophageal etiology is but one of many, although more difficult to distinguish than others. The more frequent radiation of the pain of angina pectoris to the left arm than to the right would not seem to be consistent with the possibility of radiation of pain from the esophagus itself, which should be distributed equally to both sides.

Because of the serious prognostic implications inherent in a diagnosis of angina pectoris or coronary heart disease, it is essential to emphasize the diagnostic errors that are frequently made. One source of confusion in the interpretation of symptoms of suspected cardiac disease is the so called "hiatus" or diaphragmatic hernia.

This anatomic abnormality apparently was first described by Paré in 1575. The first suggestion concerning associated symptoms was given by Morgagni<sup>3</sup> in 1769. He recounted in some detail the history of a person suffering from a "vehement

cardialgia" who was subsequently shown to have a traumatic diaphragmatic hernia. The earlier clinical descriptions of this condition were of necessity concerned with the diagnosis and symptomatology of lesions of a magnitude that could easily be noted on physical examination or by routine x-ray studies.<sup>4-7</sup> In most cases, the hernias were traumatic in origin and represented problems that were distinctly surgical. Even in 1938, Harrington,<sup>8</sup> in an excellent discussion of esophageal hiatus hernia, noted that almost two thirds of his patients had large hernias that filled the posterior mediastinal space and encroached on the left or both thoracic cavities. In the earlier clinical discussions of diaphragmatic hernia, the symptoms described were either epigastric distress or pain associated with vomiting, or intrathoracic fullness and tightness, with palpitation and dyspnea. Undoubtedly, these thoracic symptoms were due essentially to displacement of the mediastinal contents by abdominal viscera contained in the large hernial sac. Portis,<sup>9</sup> in 1925, believed that the signs and symptoms of diaphragmatic hernia were quite definite in large hernias and obscure or absent in small ones. A few years earlier, Soresi<sup>10</sup> stated that it was impossible to define the symptomatology peculiar to small hernias, although he believed that they were likely to give serious trouble. He observed that large hernias were easily diagnosed when their existence was suspected, but that small ones were frequently not diagnosed correctly and therefore were improperly treated—and even when suspected, were not always demonstrable by x-ray examination. In 1930, Moore and Kirklin<sup>11</sup> expressed the opinion that "the clinical significance of small, impermanent hernia at the hiatus, which are demonstrable only under more or less artificial conditions, has not yet been determined." Ten years later, Guthrie and Jones<sup>12</sup> noted that hernias in-

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volving only a small portion of the cardiac end of the stomach may produce more symptoms than the large ones. In the latest article on the subject, Polley<sup>12</sup> states, that no relation between the severity of symptoms and the type or size of hiatus hernia could be demonstrated.

In the earlier reports of cases of diaphragmatic hernia, histories simulating angina pectoris or heart disease were infrequent. Hedblom,<sup>4</sup> in 1925, discussing symptomatology in 378 patients, mentioned only 86 with thoracic symptoms; of these, only 19 had pain in the thorax and palpitation, and only 2 had pain in the left shoulder. Nine years later, in a review of more than two hundred articles, he<sup>13</sup> mentions dyspnea, cough, palpitation, cyanosis and intrathoracic fullness under thoracic symptomatology. He does not refer specifically to pain simulating that of angina pectoris. Healy,<sup>14</sup> in 1925, noted that substernal pain associated with regurgitation of gastric contents was common, and this symptom in association with diaphragmatic hernia has been observed in individual cases by various authors. Pain radiating into the left shoulder, upper arm and even to the hand has been similarly mentioned in single case reports.<sup>7, 12, 15-28</sup> Nevertheless, Harrington,<sup>29</sup> in a recent review, regards diaphragmatic hernia as an unlikely source of error in the diagnosis of heart disease. Polley<sup>12</sup> likewise mentions anginal pain as the least common of all the symptoms of hiatus hernia. That the manifestations of myocardial infarction may be simulated by a diaphragmatic hernia has been noted by very few. In a discussion of coronary thrombosis, Herrick<sup>30</sup> stated that he knew of only one such case. Reid<sup>28</sup> clearly describes nocturnal attacks of a severity comparable to the pain encountered in myocardial infarction.

Truesdale<sup>31</sup> stated that, in differentiating these attacks and those of angina, one may be aided by noting with the former the atypical radiation of pain to the back and its occurrence without effort and the slight evidence of heart disease. Moschowitz<sup>32</sup> admitted that 3 of his 21 patients had some symptoms resembling those of coronary disease, but stated that none had typical radiation of pain and that in none were the symptoms initiated by exertion or emotional disturbances.

Von Bergmann,<sup>33</sup> in 1932, was one of the first to exhibit interest in the relation between the pain of diaphragmatic hernia and that of angina pectoris. None of his 17 patients, however, had shoulder or arm pain, and substernal pain was noted in only 5. Interest in the possible mechanism of the pain in hiatus hernia and its effect on the heart

led him to study the so-called "gastrocardiac complex."

These divergent opinions in the literature relative to the symptomatology of hiatus esophageal hernia have led me to review in detail my experience with the disorder in private and hospital practice. The frequency with which the clinical histories of these cases suggested organic heart disease was impressive. I believe that this study throws some light on the diagnostic problem of esophageal hiatus hernia, as well as on the mechanisms involved in the production of symptoms.

#### CLINICAL MATERIAL

The material includes a series of 91 cases of small hiatus hernia and 37 cases of large hernia. Fifty of the hernias were encountered in private patients, and 78 in patients on the wards or in the Out Patient Department of the Massachusetts General Hospital. The group represents selected material only in the sense that fairly definite information was required concerning the size of the hernia, and the study included only those patients whose presenting symptoms were referable to the hernia. Patients in whom no accurate roentgenologic descriptions or exact measurements of the diaphragmatic hernias were recorded were excluded. Obviously, these criteria did not apply to a large number of patients in whom hiatus hernias were demonstrated accidentally. This seems appropriate because diaphragmatic hernias, regardless of size, may be completely asymptomatic.

The size of the hernias classified as "small" did not exceed a maximum diameter of 7 cm. Most of the cases thus classified presented x-ray evidence of a hernial sac whose greatest diameter did not exceed 4 cm. In the private cases, the average maximum diameter of the hiatus hernias was 3.8 cm., whereas measurement of the small ones taken from hospital records revealed an average maximum diameter of 4.5 cm. The reason for this difference in size is not entirely clear, but it is highly probable that the private patients came for examination sooner after the onset of symptoms than those who were studied in the hospital. All clinical evidence seems to indicate that diaphragmatic hernias tend to become slowly but progressively larger as symptoms continue. It is of interest that 9 of the private patients were examined twice before an accurate demonstration of the hernia was made, and three x-ray examinations were needed to establish the diagnosis in several patients, even though in each case it was strongly suspected. The hernias that were designated as "large," had diameters exceeding 7 cm. and con-

tained, in most cases, what was estimated to be one third or more of the stomach. No difference was noted between the complaints of patients with a so called "short esophagus" and those with para-esophageal or hiatus hernias; thus, no such differentiation has been made in this study.

As was to be anticipated from all previous reports, most of the patients under consideration were in the later decades of life and were overweight. The average age was fifty-five. A diagnosis of heart disease was considered in 24 of the 50 private patients but was finally accepted as tenable in only 13 cases after adequate evaluation of physical signs and electrocardiographic findings. Nine of the hospital cases exhibited definite cardiac abnormalities, all of which were associated with hypertension or coronary sclerosis. Because of symptoms that were at times confusing, it is noteworthy that gallstones or evidence of gall-bladder disease was present in 12 private patients and in 10 hospital patients. This incidence of heart disease and biliary-tract disease is entirely consistent with the age distribution of the patients under consideration, and corresponds with clinical experience presented in other communications on diaphragmatic hernia.

#### CLINICAL OBSERVATIONS

Of especial interest in the present discussion is an analysis of the symptoms experienced by these patients. The symptoms are considered in relation to a possible diagnosis of heart disease and particularly in relation to the diagnosis of angina pectoris. In evaluating the symptomatology associated with small hernias, special attention is directed to patients encountered in private practice, since a perusal of the records indicates that a more accurate and more detailed history was taken in this group than in the hospital group. The private patients are of special interest inasmuch as they exhibited a relatively high level of intelligence and descriptive ability.

Table 1 shows the incidence of various symptoms experienced by patients with large and small diaphragmatic hernias. Substernal pain was experienced by over one third of the 91 patients with small hernias but occurred in only 5 of the 37 with large hernias. It was more than twice as common in the private patients with small hernias as in ward patients. Shoulder pain, usually on the left, was noted in about one quarter of the patients with both types of hernia, although it appears to have been more frequent in the hospital patients with small hernias than in any of the others. The exact location of this pain was

not accurately described in the majority of records. In some cases, it was distinctly a trapezius-ridge pain, usually on the left, but in others, it was localized at the tip of the acromion process. Radiation of pain into the arm occurred in 8 of 91 patients with small hernias, 6 of whom were

TABLE 1. *Distribution of Symptoms.*

SYMPTOM	SMALL HERNIAS		LARGE HERNIAS	
	HOSPITAL PATIENTS (46)	PRIVATE PATIENTS (45)	HOSPITAL PATIENTS (32)	PRIVATE PATIENTS (5)
Substernal pain	9	25	4	1
Shoulder pain	16	8	8	1
Arm or hand pain (or both)	2	6	3	1
Palpitation	4	2	3	1
Dyspnea	7	2	10	2
Cough	0	0	0	0
Epigastric pain	31	19	21	3
Costal margin pain	16	5	10	1
Subscapular pain	0	4	0	0
Axillary pain	1	2	0	0
Back pain	12	15	9	1
Vomiting (or regurgitation)	36	15	21	3
Heartburn	1	14	1	0
Dysphagia	0	3	1	0

from the private group. Hand or finger pain was described by 5 of the latter. Four patients with large hernias noted radiation of pain into the arm, but in no case did it extend to the forearm, hand or fingers. Although the subjects usually described the sensation as pain, at times only tingling or numbness occurred. Palpitation was noted by only 6 patients with small hernias, and by 4 patients with large hernias. Dyspnea was somewhat more frequent. It was noted in one tenth of the small-hernia group and in about one third of the patients with large hernias. Curiously enough, cough and hiccough were not noted in any of the records, although these symptoms undoubtedly occur in patients with large hernias.

Epigastric pain occurred in two thirds of the hospital patients with small or large hernias, but was mentioned by only 19 of the 45 patients in the private group with similar lesions. Costal margin pain was noted on either the right or left side or both by 21 of the 91 patients with small hernias and by 11 of the 37 with large defects. About one fourth of the patients complained of pain in the back, usually in the interscapular area, and 4 of the private patients with small hernias noted pain directly under the left or right scapula. Two of the latter had gall bladder disease. Only one of all the patients complaining of pain in the back designated this as the sole symptom. In every other case, back pain was present in combination with epigastric or substernal pain. Axillary pain was noted in 3 patients with small hernias. Difficulty in swallowing was noted in only 4 cases, 3 of which occurred in patients with small hernias. Heartburn appeared to be rather characteristic of

small hernias in private patients. Fourteen of the 45 private patients complained of this symptom, whereas it was noted in the records of only 2 of the ward patients. This difference may be more apparent than real, since it was a minor symptom in many cases, and since more careful questioning might have disclosed its presence in other patients of the hospital group. Its possible importance will be discussed later.

It is noteworthy that right-sided pain involving the chest, shoulder or arm was observed by 13 of the patients with small hernias and by 6 of those with large hernias. Four of the former complained of tightness or constriction in the throat, and 2 of facial pain during severe attacks.

Bock et al.<sup>34</sup> noted the frequency of bleeding in diaphragmatic hernia. In the cases under discussion, bleeding occurred in 22 patients with small hernias and in 6 with large lesions. The evidence

this symptom. It occurred most frequently in association with epigastric or costal-margin pain in patients with large hernias. It was not uncommon, but was less frequently noted, in patients who had substernal pain or distress without epigastric discomfort. Regurgitation, rather than frank vomiting, was the rule in the group of private patients with the small lesions.

It is of especial interest in a comparison of the symptoms of diaphragmatic hernia and those of heart disease to consider initiating factors and measures that afford relief. For such a comparison, the records of the 50 private cases are in sufficient detail to warrant presentation. The findings are presented in Table 2.

Eight of 25 patients with substernal pain stated that exertion frequently initiated the symptom. When there was radiation to the shoulder, 4 out of 7 stated that exertion was a precipitating factor;

TABLE 2. Factors Affecting Symptoms Associated with Small Hernias in Forty-Five Private Patients.

SYMPTOM	CAUSE				EFFECTIVE MEANS OF RELIEF		
	EXERTION	EMOTIONAL FACTORS	EXCESSIVE FOOD	LYING DOWN	NITRO-GLYCERIN	ATROPINE	BELCHING
Substernal pain (25 patients)	8	12	15	9	8	17	8
Shoulder pain (7 patients)	4	6	4	4	3	5	0
Arm hand pain (6 patients)	3	6	3	4	3	3	3
Epigastric pain (19 patients)	4	5	13	9	3	10	5
Heartburn (14 patients)	5	4	7	3	4	7	5

of hemorrhage varied from the presence of occult blood in the stools to frank, massive hematemesis.

A consideration of the developmental pattern of these symptoms is of interest. Of the 45 private patients with small hernias, 25 had substernal pain, but only 8 had associated epigastric pain. Of the 46 hospital patients with slightly larger hernias, 9 had substernal pain, and 5 of these had concomitant epigastric distress. Only 5 of the 37 patients with large hernias had substernal distress, but 4 of these had associated epigastric symptoms. In other words, about one third of the private patients with small herniations of the stomach through the paraesophageal orifice had symptoms that were both thoracic and upper abdominal. The majority of those complaining of substernal distress, with or without radiation to the shoulder or arm, were free from abdominal symptoms. It appears, however, that patients with large hernias and thoracic symptoms had a higher incidence of associated epigastric discomfort than those with small lesions.

The frequency with which vomiting is associated with diaphragmatic hernia has been noted by all observers. In the cases under discussion, 75 of the entire group of 128 patients complained of

and in 3 of the 6 patients whose pain radiated from the substernal area through the shoulder and down the arm it was a frequent cause. It should be emphasized that *in no case did exertion invariably produce pain*, although it was frequently the important or sole cause in individual attacks. Furthermore, a careful analysis of the histories obtained from the group of private patients indicates that, without question, nervous tension and, particularly, acute emotional disturbances initiated symptoms suggesting angina pectoris. Of 25 patients who experienced substernal pain, 12 stated that emotional upsets frequently caused the symptom to appear, and when there was radiation of pain from the substernal region to the shoulder and arm, it was found that nervous tension almost invariably acted as an exciting cause. Such observations are, of course, in sharp conflict with the suggestion by Moschowitz<sup>32</sup> that typical anginal pain, especially that following exertion or emotional disturbances, is never associated with diaphragmatic hernia. By way of contrast, it is of some interest that, of 19 patients with attacks of epigastric pain, only 4 noted exertion as an inciting factor; similarly, only 5 believed that emotional disturbances played a causative role.



The intake of food, particularly of a large meal, was responsible for initiating substernal pain in 15 patients out of 25 and was an adequate stimulus for shoulder, arm and even finger pain in half the patients complaining of this type of pain radiation. Of 19 patients with epigastric distress or pain, 13 said that the symptom was frequently precipitated by eating. Somewhat less frequently, the act of lying down initiated symptoms, regardless of whether they were noted in the thorax, with radiation to the shoulder and arm, or whether they were located in the epigastrium.

Of significance also in this group of private patients is the effectiveness of certain measures used to obtain relief. Of 25 patients complaining of substernal pain, 10 received nitroglycerin in ordinary therapeutic doses, and 8 frequently obtained relief from the drug. Pain radiating to the left shoulder and arm was relieved in 3 patients out of 4 who tried it. Only 3 of 19 patients who complained of epigastric discomfort were given the drug, but all obtained some relief. It should be added that *in no case was the relief of symptoms following the use of nitroglycerin as regular as that noted in typical anginal attacks*, although at times complete relief was obtained regardless of the precipitating cause. Atropine or belladonna gave distinct relief to 17 out of 18 patients who used it for substernal distress, and all of 5 patients with shoulder pain at times obtained real benefit from its use. Similarly, 10 out of 11 patients with epigastric pain were greatly helped by atropine or one of its derivatives. Belching gave a certain temporary relief in a few patients with substernal and epigastric pain, but it did not relieve those whose pain radiated into the shoulder and arm. Various antacids were used with occasional success, but relief was not noted often enough to warrant further comment. It is my impression, however, from recent experiences with various preparations that they may afford valuable therapeutic aid.

Finally, it is germane to the discussion to comment on the infrequency with which heart disease was encountered in this study. Among the 25 private patients with small hernias who complained of substernal distress or pain, there were 6 cases of organic heart disease. Of these 25 patients, 8 had pain on exertion, but only 4 had cardiac disease. *Only one patient of the 7 who had pain radiating into the shoulder or arm had demonstrable heart disease, although 3 often noted pain after exertion.* Heart disease was not present in a single patient with epigastric pain after exertion. Among 15 patients who complained of substernal or epigastric pain following excitement,

there were only 3 who had heart disease. Of the hospital patients with large hernias, 8 experienced shoulder pain, and 1 had pain in the left arm but not in the shoulder; none of these patients had heart disease. Altogether, 15 patients with small hernias and 16 with large hernias experienced dyspnea and palpitation, yet only 4 had heart disease.

Thus, a careful analysis of the records of the 128 cases indicates that only 11 patients had heart disease that may have contributed to the presenting symptoms. Of these, 9 had the symptom of substernal pain with or without radiation. All the latter had small hernias, and the symptom was relieved in at least 3 by the use of atropine, a drug not efficacious in relieving the pain of angina pectoris. Thirty patients had substernal pain without demonstrable heart disease, and 16 others who were free of heart disease complained of shoulder or arm pain without a substernal component.

The foregoing observations direct attention to certain points. Symptoms characteristic of heart disease, such as substernal distress occasionally radiating to the left shoulder and down the arm into the little and ring fingers, were encountered frequently in patients with hiatus hernias. Exertion, nervous tension and large meals were common precipitating factors. Relief was frequently obtained by the use of nitroglycerin. Substernal distress occurred most frequently in the patients with the smallest hernias.

Certain points of difference may aid in distinguishing hernial from cardiac symptoms. Right-shoulder pain is relatively uncommon in angina pectoris. Only 1 patient with hernia and demonstrable heart disease had right-shoulder pain; this symptom, however, was noted in 19 patients with hernias in the absence of heart disease. Although exertion frequently precipitated substernal pain in the patients with hernias, it rarely did so consistently. There were notable cases in which violent exertion on one occasion would induce pain and on another would fail to do so, although dietary indiscretions and nervous tension usually precipitated attacks of pain or discomfort. A large meal or the injudicious use of alcohol frequently caused symptoms, particularly in the presence of emotional disturbances. Nocturnal attacks when the patient was in a recumbent position were not uncommon. A close relation between the onset of symptoms and the act of lying down or bending forward was noted in two fifths of the private patients and has been stressed by most observers. A further difference between the patients with hernias and those suffering from angina pectoris lies in the frequent and striking relief the former

obtained by the consistent use of atropine. Although nitroglycerin afforded dramatic relief from pain in some cases, it frequently failed.

It is apparent, then, that esophageal hiatus hernia is an important cause of symptoms, which may be confused readily with those due to serious heart disease. At times, the correct differentiation can be made only after a most careful scrutiny of all available facts, including a meticulous history. This is particularly true in very small hiatus hernias, which can be demonstrated only by extremely careful x-ray examination and then only when they are suspected. Unlike most observers, I am convinced that small hiatus hernias have a reasonably characteristic set of symptoms, which under careful observation can be properly diagnosed.

#### MECHANISM

Various theories have been advanced regarding the cause of so-called "anginal" pain. That it can occur as the result of coronary-artery disease can scarcely be doubted. When of coronary origin, it is typically initiated by exertion or sudden emotion. It is usually considered to be true referred pain<sup>35</sup> mediated over sensory afferent neurones, with which the aorta and heart are so richly supplied.

A variety of explanations have been offered for the pain associated with diaphragmatic hernia. Numerous authors have attributed dyspnea, palpitation and cyanosis, as well as the sensation of tightness in the chest, to actual displacement of the heart and mediastinal organs by the contents of the hernial sac. Such an explanation is reasonable when the hernia is large and contains a major portion of the stomach or other abdominal viscera. That the size of the hernia is active in the production of these symptoms is evident from the present study. Dyspnea was present in one third of the patients with large hernias and in about one tenth of the 91 patients with small hernias.

Aside from the effects of displacement of the mediastinum, any attempt to explain the symptoms of paraesophageal hiatus hernia must be based on a consideration of the sensory pathways included in the trunks of the vagus and phrenic nerves and in the afferent sensory neurones of the upper thoracic trunks. Von Bergmann,<sup>33</sup> in 1932, after a careful investigation of what he termed the "gastrocardiac complex," was convinced that the cardiac symptoms associated with diaphragmatic hernia were due to pressure on the vagus fibers, with consequent reflex disturbances of the coronary circulation. Jackson and Jackson<sup>36</sup> at-

tempted to prove that the pain of angina pectoris was not directly related to the heart. They believed that air or other stomach contents became trapped in the stomach or the esophagus, with resulting anginal pain. They attributed this to acute spasmodic, unco-ordinated contractions of the esophagus and stomach. This explanation seems rather far-fetched, although there can be little doubt that clinical and experimental observations have demonstrated a close relation between esophageal, gastric and cardiac functions. Morrison and Swalm,<sup>37</sup> for example, reported definite cardiac disturbances as indicated by electrocardiographic changes following balloon distention of the esophagus in patients with organic heart disease. These observations were made on patients suffering from typical anginal pain associated with heart disease, and merely prove that pain caused by intracardiac disease may be initiated by distention of the esophagus. These authors were able to show that the spasmodic, unco-ordinated movements of the esophagus and stomach described by Jackson and Jackson did not occur in attacks of angina pectoris. Kuhlmann,<sup>38</sup> Kaiser<sup>39</sup> and Kalk and Koelsch<sup>40</sup> also believed that esophageal irritation produced pain similar to angina by means of a vago-vagal reflex affecting coronary blood flow, but their findings are not conclusive. The notion that esophageal or gastric disturbances may be responsible for widespread vagal stimulation with resulting bradycardia finds ample confirmation in clinical literature and in bedside observations. That such a phenomenon in the absence of heart disease is responsible for reflex coronary constriction, which results in anginal pain in patients with diaphragmatic hernia, is more difficult to believe. The experiments of Hinrichsen and Ivy<sup>41</sup> seem to offer definite evidence against such a mechanism. Furthermore, it is the consensus among neurologists that the sensory afferent fibers contained in the vagal trunks convey few, if any, important visceral sensations except nausea.<sup>42</sup>

It seems more logical to assume that the discomfort or pain experienced by patients with diaphragmatic hernia is secondary to intraesophageal or intragastric disturbances, with typical visceral or referred pain, or to a local disturbance of the diaphragm. It is of incidental interest to refer to a rarely mentioned article published in 1887 by Dana,<sup>43</sup> who gives an excellent description of what he terms "pseudoanginal" (substernal) pain of gastric origin. His carefully illustrated article on transferred pain precedes slightly the classic article by Ross<sup>44</sup> and the later ones by Head<sup>45</sup> and Mackenzie<sup>46</sup> on referred or visceral pain. Pain stimuli

due to disturbances in the diaphragm, heart, esophagus and stomach are carried over the so-called "visceral afferent neurones" and result in so-called "viscerocutaneous pain" or referred pain. It is generally accepted that cardiac pain is mediated over the first to fifth thoracic segments, with a possible spread to the sixth. The most convincing evidence for this is the apparently established fact that bilateral section of the posterior roots of the first six thoracic nerves completely abolishes the typical pain of angina pectoris.<sup>47</sup> Pain radiating over the upper five or six thoracic segments is

Capps<sup>48</sup> has shown that pain stimuli arising from the tendinous portion of the diaphragm travel over the afferent neurones in the phrenic nerve and are distributed to the skin areas of the third, fourth and fifth cervical segments. Because of developmental variations, the distribution of the second cervical segment may occasionally become involved. It should also be noted that the fifth cervical segment includes a small area on the radial surface of the forearm just above the base of the thumb. Thus, irritation of the tendinous portion of the diaphragm typically gives shoulder

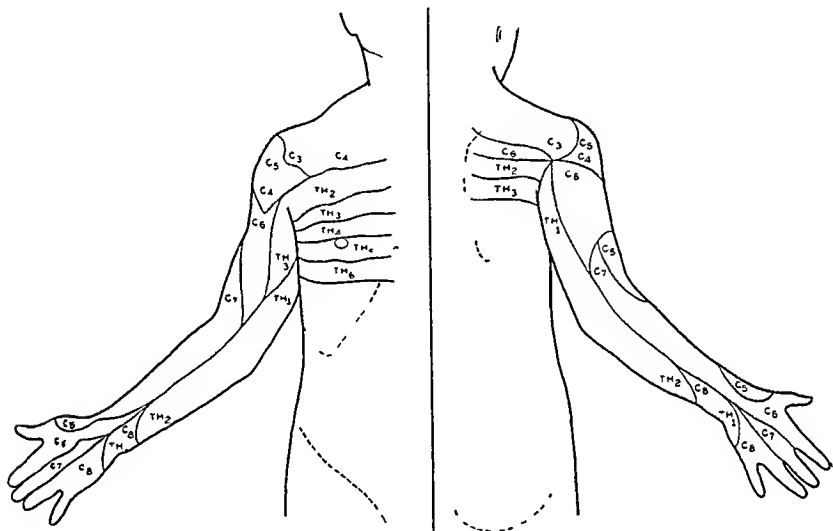


FIGURE 1 *Cervical and Upper Thoracic Dermatomes (Foerster<sup>49</sup>)*

felt over the precordium, axilla, the back from the level of the first thoracic vertebra to the sixth, and along the inner half of the arm and forearm to the base of the little finger (Figure 1). The sensory innervation of the dorsal and palmar surfaces of the little finger is included in the eighth cervical segment. Any adequate explanation of the ulnar pain of coronary origin must therefore necessitate the hypothesis that painful stimuli entering a given segment may spread beyond the original level of stimulation to one or more neighboring segments. Thus, somewhat excessive stimulation in the first thoracic segment might result in an additional area of eighth cervical reference, inducing the little finger pain so frequently noted in anginal attacks.

pain and occasionally pain in the throat, facial and nuchal regions, or pain down the arm to the base of the thumb, but never along the so called "ulnar distribution" to the little finger.

Irritation of the marginal portion of the diaphragm produces painful sensations over the segmental distributions of the seventh to the twelfth dorsal (intercostal) nerves,<sup>48</sup> an area extending from below the nipple line to the hypogastrium anteriorly, and from the midscapular region to the iliac crests or below posteriorly. Inasmuch as the attachments of the crura of the diaphragm are at the level of the first or sometimes the second lumbar vertebra, it is probable that unusual irritation of the marginal portion of the diaphragm, with traction on the crura, could be associated with

pain in the first lumbar segments, involving the hypogastrium and the area over the lateroposterior aspect of the hip. It is essential to point out that reference of pain over the middle and lower thoracic segments from the marginal portion of the diaphragm tends to be zonal in distribution and not essentially midline—that is, substernal and midepigastric.

Exact information concerning the anatomic distribution of viscerosensory fibers to the esophagus is not available. According to several careful investigators,<sup>42, 49</sup> the esophagus derives its sensory innervation from the fourth and fifth or the fifth and sixth thoracic segments. If this is true, it follows that painful sensations arising from the esophagus will be referred over the segments corresponding to the fourth and fifth (and sixth) thoracic nerves. However, it is more reasonable to believe, on the basis of embryonic development, that the afferent sensory neurones supplying the esophagus lie in the area between the first and sixth thoracic segments. In Head's<sup>45</sup> early work, he observed pain at the episternal notch in association with upper esophageal disease, and ample confirmation of this lies in the demonstration that distention of the esophagus at various levels produces midline substernal pain or discomfort at levels from the episternal notch to the xiphoid. The upper border for segmental pain referred from the esophagus would therefore be at a level well within the first dorsal segment, and any overflow from somewhat excessive stimulation might well spread over that section included in the eighth cervical segment, involving the forearm and little finger. Lateral segmental spread of painful sensations from the esophagus occurs when the stimulus is great, but ordinarily is felt only in or near the midline, in distinction to the spread of painful sensations following irritation of the margin of the diaphragm. Two other points are of significance in this connection. I<sup>50</sup> and Payne and Poulton<sup>51</sup> have demonstrated clearly that heartburn is an esophageal symptom, arising particularly from stimulation of the lower portion of the organ. Furthermore, during sudden distention with an inert suspension (barium) of the lower end of the esophagus, with resultant heartburn, it was constantly noted that spasm occurred in the cardiac end of the esophagus. At the same time, active peristalsis was seen to carry the barium suspension upward, at times as high as the upper end of the esophagus. This evidence of abnormal neuromuscular activity was invariably accompanied by a burning or painful sensation that traveled upward toward the episternal notch. Somewhat similar findings were made by Kuhlmann,<sup>38</sup> who,

as already noted, observed the appearance of substernal pain radiating into the left arm in 5 patients with small diaphragmatic hernias. This pain was found to occur when the hernial sac, which was the size of a walnut, was distended with a thick barium suspension. No cardiac abnormalities were noted while the patients were experiencing this angina-like pain, but the significant observation was made that the entire esophagus showed evidence of a marked increase in tone, increased peristaltic activity and local areas of spasm.

A useful point in localizing the source of the painful sensations in patients with diaphragmatic hernia is the frequent occurrence of marked congestion, superficial irritation and even superficial erosion of the lower end of the esophagus or of the portion of the stomach included in the hernial sac. Clerf and Manges<sup>52</sup> and others have observed such changes by esophagoscopy. They were also observed in several of my patients.

Disturbances of the fundic portion of the stomach have been shown by numerous observers to result in painful sensations referred anteriorly to the midline, subxiphoid or high epigastric region,<sup>53</sup> an area corresponding to the seventh to ninth thoracic segments.

On the basis of these considerations, it seems highly probable that the pain of hiatus or diaphragmatic hernia is mediated over visceral afferent fibers supplying the esophagus and the cardiac or fundic portion of the stomach, or over the sensory afferent fibers from the diaphragm contained in the phrenic or middle or lower thoracic nerves. Overflow to adjacent low cervical or low thoracic segments undoubtedly occurs. Overdistention of the lower end of the esophagus or the herniated portion of the stomach, with or without an associated localized esophagitis or gastritis, may thus be responsible for the production of anginal pain in any or all of its components. The shoulder pain is largely due to diaphragmatic irritation, probably by tension and traction exerted on the hernial orifice by the distended viscus contained therein. The relief obtained following the use of nitroglycerin or atropine indicates that esophageal and upper gastric disturbances are the most important components in the painful sensations experienced in this condition. This statement seems particularly applicable to the mechanism of pain noted by patients with small hernias. The role played by the vagus nerve is undoubtedly purely motor and is concerned in the production of neuromuscular disturbances, such as the spasm and abnormal peristalsis noted in the esophagus. Smooth-muscle disturbances may be initiated by a local in-

inflammatory process at or near the cardiac sphincter, by distention of the herniated portion of the stomach or by central stimulation of the esophagus secondary to marked emotional tension or excitement. In all probability, acute emotional upsets actually affect the cardiac sphincter itself, with resultant achalasia due to sympathetic (adrenergic) overstimulation. These motor disturbances are similar to those occurring in any hollow viscus and form the basis for most, if not all, visceral pain.

### TREATMENT

Treatment of the symptoms of hiatus hernia, especially those caused by small lesions, is essentially medical. Phrenicectomy or surgical repair is justified only in large hernias or when medical measures fail to give relief. A light, bland diet, taken frequently, with especial care that individual meals are relatively small in amount, is indicated. Antacids, such as aluminum hydroxide gel, are efficacious, and atropine, belladonna, Trasentan or other spasmolytics may afford additional relief during periods marked by the appearance of symptoms. Acute symptoms are frequently helped by nitroglycerin, which at times may be used advantageously before the intake of food or before retiring. The assumption of an upright or semi-upright position after eating is to be desired. Adequate rest, physical and emotional, sedation when needed and the avoidance of exercise shortly after the intake of food are also valuable measures. A further important therapeutic consideration is the proper evaluation of coronary heart disease and cholelithiasis when either condition accompanies the hernia.

### SUMMARY

A series of observations made on 128 patients with diaphragmatic hernias is presented. Especial consideration is directed to the symptomatology of this condition.

The frequency with which anginal pain due to coronary-artery disease may be duplicated by hiatus hernia is discussed.

Particular attention has been paid to the character of the symptoms observed in patients with small hernias. These symptoms are considered to be fairly typical, relatively frequent and of real clinical significance.

A discussion of the probable mechanisms involved in the production of the pain of hiatus hernia is given, and an attempt is made to clarify the routes over which hernial pain is mediated. The reasons for the similarity between hernial and cardiac pain are thus demonstrated. The points

of differentiation between pain due to hiatus hernia and that secondary to heart disease are outlined.

A summary of the medical procedures that are effective in the treatment of the symptoms of hiatus hernia is presented.

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## THE DOCTOR OF ONE HUNDRED AND FIFTY YEARS AGO\*

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THE past century and a half has witnessed greater progress in scientific discovery and invention than any other period in the history of civilization, and the science and art of medicine have kept fully abreast of progress in other fields of human endeavor and research. Medical science has utilized these discoveries for the prolongation of life and the relief of human suffering, whereas mankind as a whole has employed them in warfare for the destruction of life. I have only to cite the uses of electricity, steam, the gasoline explosive engine and discoveries in chemistry to prove these facts.

To visualize medical practice in New Hampshire in 1791, one hundred and fifty years ago, one must first form a picture of life and living conditions at that time. There were then fourteen states in the Union, Vermont having been admitted in 1790. Portsmouth was the largest city in New Hampshire. What is now Manchester was a part of the township of Londonderry. Dartmouth College was only twenty-six years old, and Dartmouth Medical School was not founded until 1798. Land travel was by horse or ox-drawn vehicle, and mostly on horseback outside the towns or along the main thoroughfares. The first New Hampshire turnpike, between Concord and Portsmouth, was opened in 1796, and the Londonderry turnpike in 1806. Light was obtained from whale-oil lamps or tallow or sperm candles. Wood was the principal fuel, and central heating was unknown.

The majority of the original members of the

Society lived in or near Rockingham County. Dr. John Rogers, however, came from Plymouth, a two days' journey from Exeter.

### MEDICAL EDUCATION AND QUALIFICATIONS FOR PRACTICE

One of the principal reasons for founding the New Hampshire Medical Society was to provide some licensing body to pass on qualifications for the practice of medicine, and the Society continued this function until the formation of the Board of Medical Examiners in 1897. Josiah Bartlett, who was the prime mover in the establishment of the Society, indulged the hope that it would do much to suppress the "dangerous host of illiterate quacks." To effect this object, he proposed that a law should be passed to prevent physicians in New Hampshire from recovering judgments in courts of law unless they had been previously examined and licensed by the Society. This, however, did not become a law.

*The American Herald of Liberty*<sup>1</sup> gives the following list of qualifications of candidates for examination before the censors of the New Hampshire Medical Society:

*Section 1.* He [the candidate] shall have a competent knowledge of the English and Latin languages.

*Section 2.* He shall have a general acquaintance with the principles of geometry and natural philosophy.

*Section 3.* He shall have studied three years under the direction, and attended the practice, of some reputable physician, or two years if he shall have received a degree at any college or university, during which time he shall have read the most approved authors in anatomy, physiology, chemistry, materia medica, surgery, and the theory and practice of physic, of all which qualifications a satisfactory certificate from the

\*Presented at the annual banquet of the New Hampshire Medical Society, Manchester, May 14, 1941.

physicians or physician with whom he studied shall be presented to the censors. Previously to his being admitted to examination, the Society earnestly recommends a university education to all designed for the medical profession, and to all students in the various branches taught in the universities.

Then follows a list of thirty-three medical books recommended for reading.

This certainly set a high standard for the physicians of that period.

The first medical school was established in Philadelphia in 1762, but most physicians obtained their education solely from preceptors. Some of the more fortunate, financially, did postgraduate work in London or Edinburgh.

The student accompanied the physician on his rounds, assisted him in operations, and compounded medicines, most of which were put up and dispensed by the doctor. Very often, the student also acted as janitor and hostler.

#### SURGERY IN 1791

Many physicians served during the Revolutionary War and obtained their surgical experience in this manner. Asepsis and anesthesia were, of course, unknown, and the closed cavities of the body—the chest, abdomen, brain and joints—were forbidden ground except in cases of accident or injury. Amputations, reduction of fractures, removal of external growths, lithotomy and cataract extraction were the principal surgical procedures.

Dr Philip Carrigan, a Concord physician, amputated a leg following an accident. Finding his saw too dull, he sent to a neighboring house to borrow a sharper instrument with which to complete his operation. The end of the bone was evidently left bare, for he picked it with a nail and applied New England rum to promote healing. On another occasion, he amputated a finger with a miller and chisel. Many of the major surgical operations at a somewhat later date were performed by "country doctors"—for example, the ligation of the common carotid artery by Dr Amos Twitchell of Keene.

Although the following story has to do with a later period than the one under consideration, it illustrates the belief in the desirability of "laudable pus." Dr E. E. Graves of Penacook sewed up a cut in a man's foot, and the wound healed by first intention. The patient, however, complained that the doctor sewed up all the "corruption" instead of allowing it to escape, and claimed that he never fully recovered from the effects of unskillful surgery. This belief in the necessity for suppuration in wound healing was the reason for the use of the

seton, which was a piece of gauze or bunch of threads or bristles introduced under the skin by a through and through incision, this formed an "issue," and the resulting suppuration was supposed to allow the escape of "peccant humours."

#### MEDICINE IN 1791

The practice of medicine at the close of the eighteenth century had evolved from what might be called the "supernatural period," prior to about 1750, when it was believed that disease was a malign agency to be exorcised by offensive substances.

Medical literature prior to this time is full of most bizarre and ludicrous prescriptions. Levine<sup>2</sup> has covered this subject so thoroughly in a recent paper that it hardly seems necessary to enter into further details in this connection. However, in the light of modern medical science, even the "witches' broth" in *Macbeth*—'eye of newt, and toe of frog, wool of bat, and tongue of dog, and so forth'—may have possessed biologic or vitamin properties.

The materia medica of this period was founded largely on roots and herbs, many of them indigenous to New England. Although the modern physician may question the value of these agents, one must remember that they doubtless made the patient more comfortable in mind and body while Nature was performing the cure, and at least most of them were harmless, which cannot be said for some recent additions to the therapeutic armamentarium. The four Herculean remedies, however,—opium, mercury, Peruvian bark and antimony,—were administered in generous doses. The classic treatment of fevers was a purge one day and an emetic the next, with an occasional and copious bleeding.

Dr Reuben D. Mussey, in his lectures at Dartmouth Medical School, gave specific instructions and indications for bleeding, and according to Josiah Bartlett's daybook, the usual charge for "phlebotomy" was one shilling.

Water, either externally or internally, was thought to be dangerous, and "night air" especially poisonous. The favorite aphorism, "stuff a cold and starve a fever," has persisted, even within the memory of some present-day physicians. A gleam of wisdom appears sometimes, however, for in Brooke's<sup>3</sup> *General Practice of Physic* occurs this sentence: "For it sometimes appears that physicians are called in to prescribe their arcana and think they have cured the disease thereby, which would have ended by the sole benefit of nature."

Diagnosis of disease was limited largely to observation of symptoms, since the ordinary diagnostic instruments—the stethoscope, the clinical thermometer and the means of urinalysis—did not appear until after the turn of the century. Much attention was paid to climate, soil, effects of diet and even astrology. Careful records were made of prevailing winds and variations in temperature in different places, especially in Salisbury, and much importance was attached to these factors in determining the course of disease.

Josiah Bartlett has left a record of success in treating what was called “cynanche maligna” (probably diphtheria), by bark and supporting measures, rather than by the more accepted treatment of bleeding and so forth. It is also a matter of record that he cured himself of a fever by drinking large quantities of cider, in defiance of his medical advisers.

It is no wonder that homeopathy, with its promulgation of an infallible therapeutic law and its substitution of small doses of the “indicated remedy” and the cold compress for the drastic measures then in vogue, was hailed by many as a revolution in medicine.

Inoculation for smallpox was the practice at that time, vaccination being not generally accepted until a later period.

A page from Josiah Bartlett’s daybook gives a picture of an average day’s work: “Benjamin French, bleeding himself. Jonathan Stevens, drawing a tooth. Elisha Winslow, calling and emetic. Elisha Batchelder, cutting child’s tongue.”

Joseph Bartlett, a nephew of Josiah Bartlett, practiced in Salisbury during the latter part of the eighteenth century. Sample extracts from his daybook give the following data:

Ensign Moses Garland to J. Bartlett, *Dr.* May 23, 1778. Bleeding Lydia D. Sleeper, 8 pence. December 4, 1778. Dressing his leg, 7 pence. January 11, 1779. A visit, *Elix. camph. opii theb., G. dracon. mag. alba. cm., Oleum anisi, etc.* and tarrying, 8 shillings.

Whether the 8 shillings was for the medicine or for the tarrying is an open question.

The polypharmacy of this era was confined to drugs; the modern physician prescribes vitamins, biologicals, vaccines and so forth *ad lib.*

Dr. Colby, also of Salisbury, was complained against because he raced horses on the Sabbath; he was so angered that he promptly left town.

Dr. Asa Crosby, later of Gilmanton, began the practice of medicine in Marlborough in 1785. Some time during the year, the authorities warned him to leave town, presumably because they were afraid he would become a public charge. He told them he would be glad to leave if they would pay his bills for professional services rendered.

This was apparently not done, since regrets were expressed by the townspeople because he had to leave.

Dr. Nathaniel Peabody, of Exeter, was imprisoned for debt for twenty years; however, he was allowed the freedom of most of the town and practiced medicine to a certain extent during that time. Dr. Stephen Tenney, also of Exeter, attempted unsuccessfully to reduce a dislocation of the shoulder; his failure so discouraged him that he abandoned the practice of medicine.

Yellow fever, which was such a scourge in other sections of the country, reached New Hampshire in only one epidemic, brought to Portsmouth in 1798 by a sailing vessel.

Influenza was epidemic at times and showed its characteristic clinical picture, with complications affecting the ears, sinuses and lungs.

“Spotted fever” was probably meningitis or typhoid fever, possibly typhus, although apparently sometimes confused with virulent influenza. “Scarlatina anginosa” was malignant scarlet fever. One is struck by the severity of its symptoms as described in medical books of the time; it is, of course, a fact that scarlet fever is much less virulent now than it was even a generation ago.

The physicians of this period were as a class more active in civic and political fields than those of the present day, largely because they were among the few men in the community with a higher education, sharing this distinction with the minister. They often engaged in the prevailing occupation of the day, namely, farming, partly as an avocation and partly to supplement the often meager income from the practice of medicine. Two of the New Hampshire signers of the Declaration of Independence were physicians, Josiah Bartlett and Matthew Thornton.

Dr. John Rogers, of Plymouth, one of the incorporators of the New Hampshire Medical Society, was a conspicuous example of public service in many fields. He was the first college-bred man in Plymouth, first postmaster, member of the first board of school supervisors, one of the founders of the Academy and register of deeds for Grafton County; he was frequently called on to preside at town meetings, and was said to have supported every public enterprise with zeal and conspicuous activity.

The old saying that history repeats itself, however, is well exemplified in the person of our present governor, who combines dairy farming, manifold civic and social activities, and a distinguished political career with the practice of medicine.

In the light of modern medical science, many of the practices of this period seem absurd. Yet many of our methods may seem just as absurd to



future medical generations. Those of us who have practiced medicine forty years or more can recall certain treatments, such as the cold-air cure for pneumonia, indiscriminate ovariectomy and the toilet of the peritoneum in cases of general peritonitis, all of which have been discarded. It is probable that the removal of tonsils, doubtless the commonest operation today, will be much modified in time to come, and some of the shotgun vitamin therapy so popular today may seem absurd to our medical successors.

The doctor of 1791 lacked the advantages of the modern diagnostic and therapeutic armamenta-

rium; he was obliged to depend almost entirely on symptoms for diagnosis and prognosis, and was a most careful observer, as attested by current medical literature. Yet he was a resourceful person, and I wonder how some of our Class A medical-school graduates would fare today if obliged to depend on their five senses as our medical forebears were.

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## INSULIN RESISTANCE IN A CASE OF DIABETES MELLITUS AND CHRONIC LYMPHATIC LEUKEMIA\*

### Report of a Case

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CASES of severe insulin resistance have been reported by many observers.<sup>1-7</sup> The maximum dose reported to date was given by Wiener<sup>8</sup> in 1938. He administered 3250 units in twenty-four hours to a fifty-eight-year-old man. No explanation for this phenomenon of insulin resistance has yet been given, although several have been suggested. We report the case of a diabetic and also leukemic patient who received 4000 units of insulin a day on four successive days. A thorough search of the literature has failed to reveal the administration of an insulin dose of this magnitude. Furthermore, the association of diabetes mellitus and leukemia has been reported in only 14 cases.<sup>9, 10</sup> Additional evidence for the infrequency of this occurrence is found in the files of the Sinai Hospital, where in over 83,000 admissions, from 1922 to 1940, these diseases were diagnosed as associated on only two occasions prior to the present case.

This case is reported, not with any hope of explaining the mechanism of insulin resistance, but because we believe this to be the largest dose of insulin ever administered to a human patient and because this is the first case of insulin-resistant diabetes in the presence of leukemia.

#### CASE REPORT

H. G., a 64-year-old Jew, was admitted to the Sinai Hospital on February 17, 1940. The patient had suffered

from hypertensive cardiovascular disease for years, and had been deaf for many years. Two years before admission, he had a complete hemiplegia. The family history was noncontributory. The illness for which the patient was hospitalized began 1 week before admission with malaise, fever and cough.

On admission, the temperature was 102.8°F., the pulse 120, and the respirations 38. The blood pressure was 200/100, and the weight 128 pounds. Physical examination revealed a moderately well-nourished and well-developed man who was acutely ill, dyspneic and cyanotic but fairly alert and co-operative. There were herpes labialis and signs of consolidation of the lower lobe of the left lung. The heart was slightly enlarged, with a loud first sound at the apex and an accentuated aortic second sound. There was marked peripheral arteriosclerosis. The abdomen was full, distended and tympanitic throughout. The liver edge, which was not tender, was palpable four fingerbreadths below the right costal margin; the spleen was palpable one fingerbreadth below the left costal margin. Multiple joints showed evidence of chronic hypertrophic arthritis. There was a residual left hemiplegia and right facial weakness. The eyegrounds were obscured by cataracts. There was no lymph-node enlargement, but the epitrochlear nodes were bilaterally enlarged. The blood showed a red-cell count of 4,240,000 with a hemoglobin of 12.6 gm., and a white-cell count of 94,700 with 20 per cent adult and 26 per cent young polymorphonuclear neutrophils, 51 per cent lymphocytes and 3 per cent monocytes. The urine showed a +++ test for sugar, but neither acetone nor diacetic acid. A serologic test for syphilis was negative. The blood urea was 62 mg. and the uric acid 4.8 mg. per 100 cc.

The patient was treated with sulfapyridine and insulin, as well as with supportive measures. The temperature fell to normal in 60 hours, and he made an uneventful recovery from the pneumonia. The blood sugar fell from the admission level of 352 mg. to 192 mg. per 100 cc. in 15 hours with the administration of 15 units of insulin, and the patient was regulated on a diet of 100 gm. carbo-

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hydrate, 60 gm. protein and 60 gm. fat, with 18 units of regular insulin twice a day. On this regime, there was no glycosuria, and the fasting blood-sugar level was 89 mg. per 100 cc. Further study of the blood revealed total white-cell counts varying from 77,000, with 76 per cent lymphocytes, to 230,000, with 86 per cent lymphocytes. At no time were any blast forms seen. The platelet count was 194,000. The basal metabolic rate was +20 per cent. A bone-marrow aspiration was interpreted as typical of chronic lymphatic leukemia. The patient was discharged on March 21, with diagnoses of lobar pneumonia, hypertensive cardiovascular disease, with cardiac dilatation and hypertrophy, old hemiplegia, chronic lymphatic leukemia and diabetes mellitus.

The patient was readmitted on August 26. Since March, he had been fairly well until 4 weeks before admission, despite a gradual weight loss of 28 pounds and the development of a painful, indolent ulcer on the left heel. Weekly fasting blood-sugar determinations during the interval averaged about 128 mg. per 100 cc. On July 31, the patient noted polydipsia and polyuria. The fasting blood-sugar level at this time was 330 mg. per 100 cc. He was treated at home with orange juice and insulin, and within a few days, the blood-sugar level was 98 mg. per 100 cc. He was then returned to his previous diet. On August 17, he showed a +++ test for glycosuria and received 130 units of insulin. Within 24 hours, the urine showed a ++ test for sugar. On August 18, the insulin was increased to 150 units a day; it was kept at this level for 5 days. This only partially controlled the glycosuria. On August 22, the fasting blood-sugar level was 350 mg. per 100 cc., and the patient was again placed on four feedings of orange juice, with four doses of insulin during each 24 hours. On August 24, the urine was sugar free, and the blood-sugar level 250 mg. per 100 cc. On August 25, the patient received 255 units of insulin in four doses, and the urine showed a + test for glucose in the evening. On the day of admission, the fasting blood-sugar level was 225 mg. per 100 cc., and the urine showed a ++ test for sugar. Physical examination on admission revealed a temperature of 99°F., a pulse of 100, and respirations of 20; the blood pressure was 210/65. The patient was poorly nourished and appeared chronically ill. There was generalized lymph-node enlargement. The fundi were poorly visualized, but the disks appeared normal; there were arteriosclerotic changes in the vessels, but no evidence of retinopathy. The tonsils were enlarged, without evidence of infection. There was a chronic superficial ulcer on the posterior aspect of the left heel. Otherwise, the physical findings were the same as those on the first admission. The blood showed a red-cell count of 4,500,000 with a hemoglobin of 14.5 gm., and a white-cell count of 63,000 with 8 per cent neutrophils, 4 per cent eosinophils and 88 per cent lymphocytes. The blood urea was 37 mg. per 100 cc., the blood uric acid was 5.2 mg. per 100 cc., and the basal metabolic rate was +31 per cent. The blood-sugar level was 327 mg. per 100 cc., and the carbon dioxide combining power was 53.2 vol. per cent. The urine showed a + test for albumin, a +++ test for sugar, a ++ test for acetone and no diacetic acid. Stereocroentgenograms of the skull revealed no abnormalities. A hip-puric acid test for liver function showed 100 per cent efficiency.

Except for congestive heart failure during the last week and persistence of the painful ulcer on the left heel, the patient was practically asymptomatic. He showed a daily evening rise of temperature to 101°F. The white-cell

count varied from 61,000 to 225,000, with 85 to 95 per cent lymphocytes, and an occasional blast was seen. The eosinophil count varied from 2000 to 8000, and on one occasion rose as high as 18,000. On September 2, the patient developed a rather marked hematuria, which persisted throughout this admission and was followed by a moderate anemia, for which the patient was transfused with 350 cc. of blood.

On admission, the patient was given his old diet of 100 gm. carbohydrate, 60 gm. protein, 60 gm. fat. During the first 24 hours, he received 100 units of insulin, but the blood sugar remained above the admission level. For the next 48 hours, 2080 units were required. At the end of this period, the blood-sugar level was 109 mg. per 100 cc., and the patient developed hypoglycemia, with symptoms; insulin was omitted for 16 hours. Beginning August 29, insulin was gradually increased for 15 days until the patient received 4000 units in 24 hours, 800 units of which were protamine zinc insulin. He received this dose for 4 days, during which the blood-sugar levels varied between 200 and 450 mg. per 100 cc. On September 17, the amount fell to 66 mg. per 100 cc., and the patient again developed symptoms of hypoglycemia. The insulin dosage was reduced, and for 3 days he received from 1100 to 1300 units a day, the blood-sugar levels varying from 66 to 356 mg. per 100 cc. On September 20 and 21, 3100 units of insulin were administered each day, and the amounts of blood sugar ranged from 344 to 476 mg. per 100 cc. On September 22, the patient had a marked hypoglycemic reaction after receiving 2000 units, which was treated with intravenous glucose. During the next 24 hours, the blood-sugar levels averaged about 60 mg. per 100 cc., and he received 300 units of insulin. For the next 8 days, the insulin requirements gradually rose again, until on September 30 and October 1, he received 3200 units a day, with blood-sugar levels ranging from 400 to 500 mg. per 100 cc. Another hypoglycemic phase ensued for 4 days. Insulin was withdrawn for 96 hours, and carbohydrate administered by mouth and vein. This was the only occasion on which the patient developed generalized hypoglycemic convulsions. On October 4, he began to show signs of congestive cardiac failure. On October 7, the hypoglycemia ceased, and the blood sugar began to rise again. Insulin was administered in moderate doses, but despite this and other treatment, acidosis supervened and congestive cardiac failure progressed. The patient died on October 11, 6½ weeks after admission. Permission for autopsy was not obtained.

## DISCUSSION

This case is of interest because of the size of the insulin dose and the coincidental occurrence of leukemia.

The patient received 76,195 units of insulin in forty-seven days, or an average of 1621 units every twenty-four hours. During this entire period, he was under hospital conditions and at complete bed rest. The insulin was obtained from several different sources, and included 1280 units of zinc insulin crystals and 9950 units of protamine zinc insulin. Insulin from different sources was used to exclude the possibility of an inactive lot of insulin and of allergic reactions to animal insulins.

Two recent articles<sup>11, 12</sup> have thoroughly reviewed the subject of insulin resistance and the

many suggestions that have been made concerning its mechanism. The general conclusion in both these articles is that nothing is known that will satisfactorily explain such a high degree of insulin insensitivity.

Root and Carpenter<sup>13</sup> have approached the problem of insulin resistance by the determination of respiratory quotients to study the metabolism of glucose in diabetic patients under various conditions. In uncontrolled diabetes, the fasting respiratory quotient is low, but rises rapidly to normal

kemia, persistent eosinophilia and an indolent ulcer of the left heel.

The increase in insulin requirement, occasioned by complicating infection, never reaches the proportions attained in this case even in the presence of severe acute infections, and this superficial chronic ulcer can therefore be excluded as a possible cause of the insulin resistance.

The eosinophilia is worthy of comment only because several cases previously reported<sup>14, 15</sup> exhibited insulin resistance associated with allergic

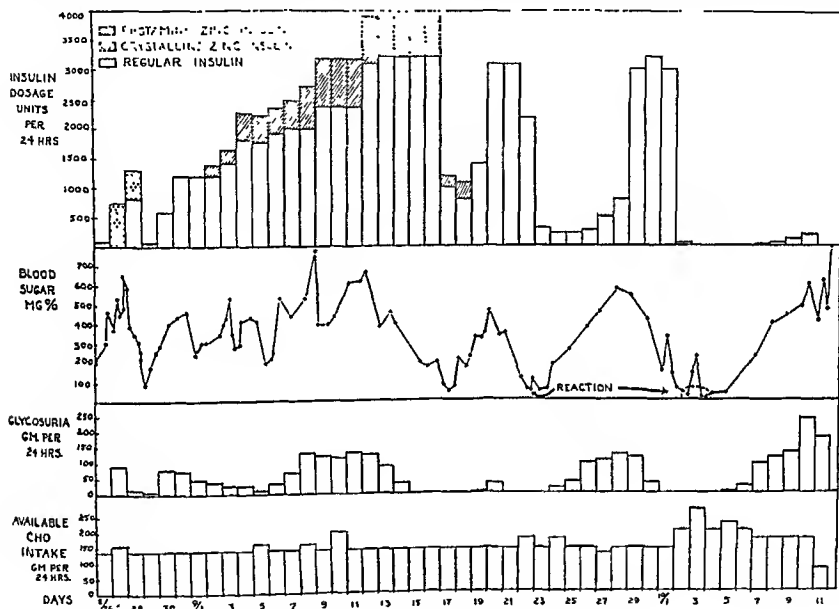


FIGURE 1. Summary of Clinical Data.

after a few days of insulin therapy. Patients under insulin treatment show a rise in the fasting level of the respiratory quotient if the amount of carbohydrate in the diet is increased. In cases of insulin resistance in which insulin efficiency is seriously impaired, the respiratory quotient can be raised to a normal level if sufficient insulin is given. This indicates at least a partial correction of the disturbed carbohydrate metabolism. In addition, Root and Carpenter point out the cyclic character of insulin resistance, which this case demonstrates so well.

Although no necropsy was performed on this patient, clinical study revealed no evidence of pituitary or hepatic dysfunction. The only complicating conditions that might have been related to the insulin insensitivity were chronic lymphatic leu-

kemia. There was no other evidence of allergic reaction to insulin in the present case, and no definite correlation between the insulin dose and the eosinophil level.

Review of the 14 reported cases of associated diabetes mellitus and leukemia reveals 4 cases of chronic myeloid leukemia, 8 cases of chronic lymphatic leukemia, 1 case of acute myeloid leukemia and 1 case of monocytic leukemia. The 2 patients previously observed at the Sinai Hospital had chronic myeloid leukemia.

The association of insulin-resistant diabetes and leukemia raises the interesting possibility that the increase in blood leukocytes may have some effect in reducing the efficiency of insulin. In 1933, Bürger and Kohl<sup>16</sup> demonstrated the presence of

an anti-insulin substance in the leukocytes of leukemic blood. This substance possessed a trypsin-like activity. Several observers have suggested the presence of an anti-insulin substance in the blood or tissues of leukemic patients. Although no attempt was made to demonstrate the presence of insulin inactivating substances in this case, this mechanism is mentioned as a possible explanation. Against this hypothesis is the absence of insulin resistance in any of the previously reported cases of diabetes associated with leukemia.

### SUMMARY

A fatal case of extreme insulin-resistant diabetes associated with chronic lymphatic leukemia is presented. Seventy-six thousand, one hundred and ninety-five units of insulin were administered in forty-seven days. On four successive days, the patient received 4000 units in each twenty-four hours.

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## MEDICAL PROGRESS

### LEUKEMIA: AGRANULOCYTOSIS\*

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#### LEUKEMIA

WINTROBE and Mitchell<sup>1</sup> once more, and very properly, emphasize the facts that any organ of the body may be involved in the leukemic process and that the initial symptoms of leukemia may therefore be of the most varied sort. These authors write, "Such different disorders as acute thyroiditis, osteomyelitis, tuberculosis, pelvic tumor, subacute bacterial endocarditis, infection of the eye, breast tumor, gallbladder disease, coronary thrombosis, paroxysmal tachycardia and brucellosis were considered when the patient was first observed because the clinical pictures were so suggestive of these diseases." To this list could be added many more conditions—especially, obscure oral sepsis, rheumatic fever and acute appendicitis. Most of their cases were examples of

acute or subacute leukemia. However, the protean character of the chronic as well as the acute leukemias and of the leukemoid states can scarcely be overemphasized. Without a full appreciation of the vagaries of these conditions, the proper diagnosis may be missed when it could otherwise be easily made.

The bone changes seen in patients with acute leukemia are again stressed by Mendl and Saxl,<sup>2</sup> who described the following: a local proliferation in the bone marrow, with erosion of the bone trabeculae and subsequent cavity formation; periosteal proliferation; and increased bone formation about the cavities mentioned above. Such changes are particularly apt to be seen in children; they are uncommon in adults. Their detection may lead to a correct diagnosis of leukemia in cases with atypical blood pictures; on the other hand, such lesions may give rise to symptoms closely simulating those of rheumatic fever and may therefore lead the clinician astray unless he is aware of their true significance.

All articles in this series will be published in book form: the current volume is *Medical Progress: Annual, 1940* (Springfield, Illinois. Charles C Thomas Company, 1941. \$4 00).

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Moloney<sup>3</sup> once more emphasizes the importance and frequency of mouth lesions in acute leukemia. This aspect of leukemia is of great significance to the oral surgeon and the dentist, as well as to the internist; in fact, some oral surgeons always do a complete blood study on any patient with an obscure oral lesion—a very wise precaution.

It is now increasingly well recognized that many pathologic conditions may give rise to hematologic pictures very closely similar to those of true leukemia,<sup>4</sup> and recently Jackson, Parker and Lemon<sup>5</sup> have described a series of cases that from both a clinical and hematologic viewpoint resemble either hemolytic anemia or chronic myelogenous leukemia. It was not the intention of these authors to define and describe a new disease but rather to delineate a clinical and pathologic syndrome that was, in their opinion, worthy of separation from the hemolytic anemias and the leukemias simply because the usual therapy of these conditions—splenectomy and irradiation, respectively—usually brought about speedy death in the disease that they describe as agnogenic myeloid metaplasia. The condition runs a chronic, comparatively asymptomatic course. The spleen is often greatly enlarged. A past history of mild polycythemia may be elicited. The red cells are frequently abnormally fragile, and show a marked variation of size and shape. Nucleated red cells out of proportion to the degree of anemia present are often seen, and there is almost always a definitely leukemoid type of white-cell reaction. The bone marrow may be fibrotic, aplastic, normal or hyperplastic; it never shows the characteristic features of true leukemia. The fibrotic spleen shows scattered areas of erythropoiesis and myelopoiesis, but the Malpighian corpuscles are for the most part intact, and the diffuse sheetlike infiltration so commonly seen in leukemia is absent. The relation of this syndrome to true leukemia, hemolytic anemia, polycythemia and benzol poisoning must remain *sub judice*. It is possible that certain industrial solvents play a role in its initiation.<sup>6</sup>

The treatment of acute and chronic leukemia still remains unsatisfactory.

It is the general consensus that patients suffering from acute leukemia should be treated for symptoms only.<sup>7</sup> As Lucia<sup>8</sup> states: "It is more valorous to be conservative in the treatment of acute leukemia. It is rarely benefited by any sort of treatment." I heartily agree: with the obvious reservation that symptomatic treatment—especially transfusion to combat bleeding—is clearly indicated so long as it is possible to alleviate the patient's distress by nonspecific measures.

Those agents commonly used to combat chronic leukemia are either useless or dangerous.

For patients with chronic leukemia,—of whatever sort,—irradiation still remains the treatment of choice. Lucia<sup>8</sup> has admirably summarized present-day knowledge—or lack of it—in this respect. He believes that treatment should be considered: when the leukocyte count is over 200,000; when the effects of mechanical pressure produce symptoms; when there is a marked and progressive anemia; when weight loss is a prominent factor, and especially when it is due to gastrointestinal dysfunction; when there are hemorrhagic manifestations; when the temperature remains elevated; and when the basal metabolic rate is high. He expressly states, "Do not treat a leukocytosis." I take this to mean that he would not treat a patient with leukemia who had a high white-cell count but who had no complaints whatever. This seems to be a conservative view. Unfortunately, there are few such patients—particularly in the myelogenous group. It has been for a long time my own opinion that any patient with chronic leukemia who has any symptoms properly referable to the disease—be they ever so slight—should be treated. The majority of those interested in this field agree on this point. On the other hand, it is the sincere and carefully considered opinion of some workers that *completely* asymptomatic cases of chronic leukemia do not need specific treatment.

There is a growing belief that the smallest dose of x-ray that will produce the desired result is the best. Dowdy and Lawrence<sup>9</sup> believe that each case should be individualized and that initially from 25 to 50 r should be directed to the spleen, to the involved nodes or to quadrants of the body, and that further treatments should be given as indicated by the patient's course. These investigators give daily doses as required but properly warn that a rapid decrease in the white-cell count necessitates an interruption of the treatment until the count has become stabilized. This latter point needs especial emphasis. The routine, uncontrolled continuance of any form of x-ray therapy may result in a dangerous degree of leukopenia—even death. One cannot predict in advance how much irradiation will be required, and it may seriously be questioned whether daily doses—even though small—are entirely safe in all cases. The white-cell count in patients with leukemia occasionally falls with great rapidity days or weeks after the last treatment, even though this was as small as 25 or 50 r.

Murphy,<sup>10</sup> writes, "The most obvious and serious fault [of treatment] appeared to be that of

allowing the patient to develop repeated relapses during which the disease has progressed followed by intensive treatment at a time when the general condition is poor." That practically every investigator in this field has done his best to avoid this sequence of events need hardly be pointed out. Murphy goes on to state that there is a "belief held by many clinicians that the patient with chronic leukemia is not in better condition with a low than with a high leukocyte count." "It is quite obvious," he says, "that with the method of therapy often employed such might be the case. Massive x-ray dosage is applied over the spleen at a time when the patient is weakened after suffering from anorexia and nausea and with a high leukocyte count." "Massive x-ray dosage," in the true sense, should *never* be used in patients with leukemia, and treatment should always be instituted as soon as symptoms of whatever sort appear. Treatment should *never* be withheld until the patient's general condition is poor and his efficiency low. To do so is to court disaster. Few students of the disease would be so bold. Murphy, himself, advocates 50 to 60 r at a time to the entire body by the spray technic. This general scheme of treatment seems reasonable. Yet 50 r spray may in certain cases be too large a dose, and certainly Reznikoff<sup>11</sup> is correct when he warns that "it is important to determine therapy not on any routine but on what the patient shows at the particular time and how the patient responds to the particular therapy at a time."

It is possible that spray irradiation to the entire body at appropriate intervals (weeks), with due regard for the patient's signs and symptoms and his total red-cell and white-cell counts, is the most effective treatment today. It may further be necessary to give regional treatments to the spleen or greatly enlarged lymph nodes; for the latter are not infrequently entirely unaffected by spray irradiation even though the total white-cell count is greatly reduced and the patient's general condition apparently improved.

It is curious that so few investigators refer to the red-cell count or its bearing on the general situation. The problem of leukemia—with certain obvious limitations—resolves itself into the maintenance of a reasonably normal red-cell count rather than the reduction of the white-cell count to certain arbitrary levels. The inestimable value of transfusions in chronic leukemia is seldom stressed. It should be. More than one patient has been kept alive and at his usual work for long periods by repeated transfusions, without irradiation of any sort. Furthermore, no patient should be given irradiation therapy if marked anemia is present,

even though in general such treatment, by partially freeing the bone marrow of the abnormal white cells, may have a beneficial effect on erythropoiesis. Several transfusions may be necessary to raise the red-cell count to a level at which irradiation may be safely and beneficially given.

The role of radio-phosphorus in the treatment of leukemia has yet to be fully evaluated. It is clear that such substances should be tried under proper conditions by physicians conversant with the disease. It is equally clear that this form of therapy should not yet pass into general use or be regarded as definitely superior to other forms of irradiation. Lawrence<sup>12</sup> concludes that it is too early "to estimate fairly this form of therapy." Erf, Tuttle and Lawrence<sup>13</sup> give a very complete discussion of the use of radio-phosphorus in leukemia and consider that it "is as effective as other types [of treatment] in general use, can be easily administered orally or intravenously, produces no nausea, weakness or anorexia . . . and the results are sufficiently encouraging to warrant intense investigation." One might perhaps substitute the word "critical" for "intense." According to these authors, acute leukemia does not respond any better to radio-phosphorus than to any other form of therapy.

#### AGRANULOCYTOSIS

It is now common knowledge that the great majority of cases of agranulocytosis are secondary to some drug, but I am inclined to agree with Drevierman and Gardner<sup>14</sup> that some are truly idiopathic. Furthermore, it has long been recognized that severe neutropenia indistinguishable from the classic agranulocytosis may be secondary to overwhelming sepsis. In practice, it is difficult, if not impossible, to distinguish between idiopathic agranulocytosis and the leukopenia associated with certain drugs, overwhelming sepsis and industrial poisons. The term "agranulocytosis," as used in this article, is therefore not restricted to the classic definition, but includes states of extreme leukopenia and neutropenia associated with the above-mentioned conditions.

Aminopyrine is now less often a provocative cause, for the simple reasons that the dangers of this drug have become rather widely appreciated and that the sale of the drug is limited by law, but it must be remembered that aminopyrine may be an ingredient of many of the lesser known sedatives and analgesics, and one should be extremely cautious before administering such therapeutic agents unless their composition is definitely known and attested. Several fatal cases of agranulocytosis have followed the administration of Causa-

lin,<sup>15, 16</sup> and without much question many more such cases due to similar drugs of uncertain composition have occurred but have not been reported.

Preparations containing gold are an occasional cause of agranulocytosis. This subject has been recently reviewed by Anderson and Palmer.<sup>17</sup> It should be remembered that some of the pathologic states for which gold salts are administered may in themselves be attended by severe and perhaps fatal leukopenia.

With the ever-increasing use of the sulfonamide compounds, an increasing number of cases of agranulocytosis are directly traceable to these drugs.<sup>18-22</sup>

In a series of personally collected cases, 109 followed the use of some drug. Thirty-four followed sulfanilamide, 8 sulfapyridine, 39 aminopyrine, 7 Allonal and 4 Causalin. In decreasing frequency, the following drugs were apparently causative: Cibalgine, Acetanalid, Amidophen, cinchophen, Amytal Compound, Bismarsen and neocinchophen. It is probable that any of the sulfonamide compounds may cause agranulocytosis; hence, the disproportionately large number of cases that are reported after sulfanilamide is perhaps due to the fact that this drug has, so far, been more widely used than any other of the series. Hadler<sup>23</sup> reports a case apparently due to Allurate; the patient recovered following the use of Pentnucleotide and Reticulogen. This single case report raises the serious question of whether agranulocytosis may not be brought on by barbiturates, heretofore considered blameless.

It is essential to remember, as Rinkoff and Spring<sup>21</sup> point out, that fatal agranulocytosis may follow even small doses of any of the incriminated drugs, and all should therefore be used with the greatest caution. I agree with these authors that such therapeutic agents should seldom be used prophylactically, and it may seriously be questioned whether aminopyrine should ever be used except as an analgesic in patients suffering from incurable disease.

The treatment of agranulocytosis still remains a matter of debate. Forkner<sup>24</sup> appears to regard all forms of therapy as useless. Such pessimism does not favor the acquisition of further data regarding the therapeutics of a disease admittedly fatal in some 70 per cent of the cases. On the other hand, Goldhamer, Sturgis and Bethell<sup>17</sup> write: "We do not agree with Forkner in labelling as useless all forms of treatment which have been suggested for agranulocytosis. It is . . . [our\*] opinion that there does exist evidence which sug-

gests strongly that pentnucleotide and blood transfusions are superior to other forms of therapy and should be employed in all cases." Others<sup>14</sup> recommend Pentnucleotide and yellow bone marrow, both of which agents, in their opinion, play a role in the maturation of the white cells. Strong,<sup>25</sup> discussing 3 cases of granulopenia apparently due to infection, states:

Although the discontinuance of the therapeutic agent [sulfonamide compound] is probably the only measure necessary when the granulocytes reach a low level, pentnucleotide appears to accelerate the rate of recovery of the bone marrow, and this drug may prove to be a useful therapeutic addendum for us with young patients. A combination of attempts to control the infection, discontinuance of drugs which may affect [adversely] the bone marrow, the use of frequent transfusions and the administration of pentnucleotide seems the logical form of treatment.

The question of the administration or continuance of the sulfonamide compounds in the presence of extreme leukopenia must be a matter to be decided in each case. Three points, however, seem clear. Firstly, if the agranulocytosis is patently or probably due to the drug, the latter should be summarily stopped. Secondly, if the agranulocytosis is obviously caused by an infection ordinarily amenable to treatment with the sulfonamide compounds (for example, pneumococcal pneumonia), these therapeutic agents should be immediately started together with such other measures—for example, Pentnucleotide—as the physician in charge believes may help restore the white-cell count to normal levels. Thirdly, the mere withdrawal of the offending drug does *not* always suffice to restore the white-cell picture to normal, especially if the leukopenia and granulocytopenia have been extreme, in spite of a rather general belief that withdrawal is sufficient. Such optimism is based largely on reports of cases with moderate leukopenia (for example, 3000 white cells, of which 20 per cent were polymorphonuclear neutrophils). In 72 personally collected cases of extreme agranulocytosis (without anemia of moment) due to sulfonamide compounds or other drugs, recovery occurred in but 30 per cent of those in which withdrawal of the drug was the only measure taken. In 26 similar cases in which the drug was withdrawn and adequate amounts of Pentnucleotide (40 cc. a day) were given, recovery occurred in 66 per cent. The series is small, but the results are suggestive. In any event, daily white-cell and differential counts should be done on all cases suspected of having agranulocytosis, and energetic measures should be immediately started if the diagnosis is established.

\*Personal communication from Dr. Cyrus C. Sturgis correcting a misprint in the article.

If one has faith in any of the therapeutic measures advocated, the value of prompt diagnosis and treatment cannot be overemphasized. If one maintains a robust pessimism, the acquisition of hematologic data is purely of academic interest. It is my own belief—and it is shared by others—that all patients under treatment with any drug that has been incriminated should have frequent blood-cell and differential counts and that if the total granulocyte count is found to be very low, immediate treatment should be instituted—whether one chooses Pentnucleotide, frequent transfusions, yellow bone marrow or a combination of two or more treatments. The same principle holds true of patients with a severe sore throat, perhaps the commonest initial symptom of agranulocytosis. It is furthermore imperative that treatment should be intensive—with Pentnucleotide, no less than 40 cc. a day should be given and continued until a favorable response has occurred or until it is apparent that no benefit will accrue.

It is perhaps worth pointing out that those measures designed to combat agranulocytosis will not benefit patients with aplastic anemia or those with aleukemic leukemia, both of which conditions may be confused with agranulocytosis. But it is equally important to note that these therapeutic agents can do no harm in such cases. If there is the slightest doubt concerning the diagnosis, the patient should be treated as a case of agranulocytosis.

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# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M.D., *Editor*

## CASE 27511

### PRESENTATION OF CASE

A dirty six year-old physician was admitted to the hospital because of a long history of recurrent pneumonia," treated in several different outside hospitals

Twenty two years before entry, the patient had epidemic influenza, with probable left sided pleurisy After recovery, he was in good health for six years Then, while in college, following an upper respiratory infection, he developed pneumonia of the left lower lobe, which resolved slowly over a period of three months From that time on, he felt "rundown" Fifteen years before entry, while in his first year at medical school, he again had an extended attack of "left lower lobe pneumonia," following an upper respiratory infection, there was slight hemoptysis at the onset In the later stages of the illness, the patient coughed up pus Several chest taps failed to reveal fluid A rib resection was considered but not under taken He was fairly well for about three months, only to have another similar episode, a productive cough remained after the other symptoms had cleared He was therefore bronchoscoped, and an "obstruction" removed from the bronchus to the left lower lobe Microscopic sections were said to have shown bronchiogenic carcinoma or granuloma Subsequent bronchoscopies were performed at lengthening intervals, with occasional application of iodine to the site of the former obstruction This course of treatments brought marked improvement, and the patient was quite well for several years In a check up examination two years later, an instillation of lipiodol was said to have shown some left lower lobe bronchiectasis, but no obstruction A bronchoscopic check examination, ten years later, was considered essentially negative During this long interval, the patient remained quite well Then, seven months before entry, he again went through the sequence of upper respiratory infection, slight hemoptysis and "left lower lobe pneumonia," lasting about a month After the acute phase of the illness, he remained somewhat tired A roentgenogram of the chest showed the heart shifted to the left, and the lung fields fairly clear About

four months before entry, another respiratory infection was followed by slight hemoptysis and left lower lobe consolidation The temperature spiked to 102°F for about a month The patient was bronchoscoped at least ten times, with removal of a left lower lobe obstruction," and subsequent drainage of pus Convalescence was gradual, with reduction in the temperature and the amount of sputum coughed up Most of the 30 pounds of weight lost during the active phase of the illness was regained In the few months preceding entry, the patient felt fairly well, between recurrent bouts of fever up to 101°F, which lasted four or five days and were associated with severe night sweats The sputum averaged 3 or 4 tablespoonfuls a day

The family history was not of interest, except that the patient was one of twins Prior to the onset of his series of illnesses, he had been quite athletic and active He said that he was "allergic" to a number of substances, including iodides

On admission, the patient appeared strong and well developed, with a moist skin that seemed pale although tanned The trachea and heart were shifted to the left The heart was otherwise normal There was dullness posteriorly over the area of the left lower lobe, with bronchial breathing, increased whispered and voice sounds, and decreased tactile fremitus There were no rales The diaphragm was high on the left side, but showed good excursions on the right The abdomen was normal The fingernails were slightly ridged, but were not clubbed

The temperature was 98.6°F, the pulse 78, and the respirations 20 The blood pressure was 134 systolic, 74 diastolic

Examination of the blood showed a red cell count of 5,050,000 with 15.3 gm hemoglobin, and a white cell count of 11,800 with 68 per cent polymorphonuclears The blood Hinton reaction was negative The serum protein was 5.6 mg per 100 cc The urine was normal Culture of the sputum grew alpha hemolytic streptococci

A roentgenogram of the chest showed slight elevation of the left diaphragm, with limited paradoxical motion The left lower lung field was evenly dense, up to the level of the third rib anteriorly There was questionable narrowing of the left lower lobe bronchus The left hilus was placed low The mediastinum was displaced markedly to the left, with a shift in that direction on inspiration The upper part of the left lung field was bright, and the right lung field was clear Another roentgenogram of the chest, five days later, was essentially similar

An electrocardiogram was normal except for a tendency to slight left axis deviation

On the seventh hospital day, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. RALPH ADAMS\*: The outstanding characteristic of this history is the symptomatology associated with recurrent episodes of localized pulmonary infection over a sixteen-year period in a young man who was otherwise in good health. Since chronic pulmonary infection is always a suppurative process, differential diagnosis should be concerned with only two problems: the nature of the infection and its primary cause. I shall discuss the type or nature of the infection before its cause, since that is the sequence in which pulmonary disease is considered clinically, the presenting symptoms being based on an etiology that is rarely, in itself, manifest.

The influenza from which the patient suffered at the age of fourteen, twenty-two years before entry, during the great influenza epidemic of 1919, I am inclined to accept as diagnosed because it is not statistically unlikely that he should have had the disease in that year, and because his subsequent good health for the next six years seems to classify it as an isolated case of acute infection and recovery. Then, at the age of twenty, sixteen years before entry, he had an attack of so-called "left-lower-lobe pneumonia," which required three months to resolve, and left him rundown. Pneumonia that requires three months to resolve either has been complicated by unrecognized empyema or is not true pneumococcal pneumonia. Barring empyema, the cause is more likely to be lung abscess or pneumonitis secondary to bronchial obstruction.

A year later, the patient had a second extended attack of left-lower-lobe pneumonia, accompanied initially by hemoptysis and terminally by pus. The common reasons for hemoptysis are categorically easy to state, although selection of the proper reason in a specific case may require much analysis and more or less specialized methods of diagnosis, such as bronchoscopy and the injection of iodized oil. Hemoptysis implies mechanical injury, invasion, ulceration or necrosis of some part of the bronchial mucosa, and may be secondary to a foreign body, a benign or malignant tumor, infections like bronchiectasis and lung abscess, or lack of oxygenation of the tissues from infarcts or advanced mitral stenosis. I must add a small group in which one simply cannot determine the cause of the bleeding. All thoracic clinicians have encountered them. The late appearance of purulent sputum in this case indicates that an infection was instrumental in causing the hemoptysis. Em-

\*Surgeon, Lahey Clinic.

pyema was suspected, and unsuccessful chest taps ensued, undoubtedly done after the misinterpretation of the x-ray shadow of lobar consolidation or collapse as pleural fluid. This is a common error and carries the hazard of producing the disease it is designed to detect. Another common reason why a chest tap may fail to reveal fluid is that the needle is inserted too low in the chest. The next episode, three months later, was followed by a productive cough, and this sign must be added as another bit of evidence in the case that I am building for chronic bronchopulmonary suppuration.

At this time, two years after the onset of the disease and fourteen years before entry, the patient was bronchoscoped, and an "obstruction" removed from the left-lower-lobe bronchus. I am left to guess what the obstruction was, and for the delectation of this audience it is of course hoped that I shall guess wrong. Again, speaking generically, the varieties of bronchial obstruction are easy to classify. They may come only from without or within the patient. If from without, they are, *ipso facto*, foreign bodies; if from within, they are benign or malignant tumors, liquid or inspissated secretions, or stenosing processes secondary to infections or pressure. Here, as in cases of hemoptysis, decision in terms of the individual patient is more difficult than textbook enumeration. I shall discount completely the microscopic report of bronchiogenic carcinoma, which when untreated is incompatible with a subsequent life of fourteen years. In spite of alleged evidence in the literature to the contrary, most tumors with microscopic diagnoses of bronchiogenic carcinoma made in patients found to be alive several years afterward without surgical intervention have proved, on critical review of the slides, to be benign adenomas of the bronchus. The bronchial application of iodine is neither recommended nor believed to be helpful therapy. Iodized-oil instillation two years later in this patient revealed bronchiectasis, and thus completes the data on the nature of the intrapulmonary process.

I shall try to determine the primary cause of this process. Carcinoma has been excluded. Except for the check bronchoscopy some years after the first, I find it troublesome to exclude a benign adenoma, because many of the criteria for adenoma have been fulfilled: there was bronchial obstruction, with repeated slight hemoptyses; there were frequent episodes of pneumonitis; there was proved bronchiectasis peripheral to the observed area of obstruction; and by x-ray films, the heart was shifted toward the lesion. But the obstruction seen at the first bronchoscopy was gone at the

second Adenomas do not disappear, they grow larger, and the extrabronchial growth is often disproportionate to the intrabronchial, causing both intrinsic occlusion and extrinsic pressure. This situation could hardly have been missed. Therefore, I am forced to say that the patient did not have an adenoma, and that the subsequent bronchoscopies were only for removal of pus. Since the iodized oil injection, the second bronchoscopy and, finally, the x-ray films showed no bronchial obstruction at the later date, the possibilities are reduced to inspissated secretion and a foreign body surrounded by inflammatory tissue to explain the obstruction that the first bronchoscopist removed and the pathologist diagnosed as a "bronchiogenic carcinoma or granuloma." I doubt if anyone could mistake a mucous plug for a carcinoma, but organic foreign bodies, particularly, can produce a violent bronchial reaction. I am now left supporting the proposition that the original obstruction removed bronchoscopically was a foreign body that was misdiagnosed, and that all the succeeding illness was a sequel in the irreparably destroyed lung peripheral to the obstruction. It seems that a boy of twenty would know whether he had inhaled a foreign body, and have said so for the record, and here is the weak point in the circumstantial evidence as arrayed. However, I can do no better and shall let the cause of obstruction rest as a foreign body until Dr Mallory discards it.

The physical and x-ray findings in the chest were typical of the pathologic process as postulated—that is, a collapsed chronically infected left lower lobe, with compensatory emphysema of the left upper lobe and a shift of the mediastinal structures and diaphragm. I cannot explain the paradoxical diaphragmatic movements described, unless the patient had had a surgical phrenic paralysis at some time in his therapeutic course.

May we see the x-ray films?

DR AUBREY O. HAMPTON: These are selected films that show marked displacement of the heart to the left. With barium in the fundus of the stomach, one can see that the diaphragm is elevated. There is a shadow that rises in the left axillary line, and the whole lower portion of the left lung is dense. The size and shape of the shadow is not the picture we see in uncomplicated collapse of the left lower lobe. The band of density along the left axillary line is not compatible with simple collapse but is compatible with collapse and pleurisy. Here is another in compatible feature, that is, a shadow at the lung root, which is convex upward. I do not know

the answer to this. Here are dilated bronchi, so that bronchial occlusion is not complete, but there is no other air in the lower lobe.

DR ADAMS: When I started the discussion, I felt insecure in my analysis of the cause of obstruction, which I had based more than I liked on the pathology as reported and as not reported. After seeing these films, I must admit that a benign adenoma of the bronchus is just as likely as an old foreign body, and I really do not know which to place first. I am prepared now to reverse myself. My diagnosis in this case is bronchiectasis, chronic recurring pneumonitis and peripheral pulmonary suppuration with old bronchial obstruction, probably due to a primary benign adenoma.

DR WILLIAM B. BREED: I should like to ask why Dr Adams surrendered the foreign body hypothesis so quickly. Was it entirely on the basis of the x-ray films?

DR ADAMS: Yes, the x-ray film is the most important diagnostic feature in thoracic disease, I believe, and I had not had the benefit heretofore of seeing the films. Having seen them, I should go so far as to say that this is the classic picture of adenoma of the bronchus.

#### CLINICAL DIAGNOSES

Adenoma of left lower bronchus  
Bronchiectasis

#### DR ADAMS'S DIAGNOSES

Bronchial adenoma  
Bronchiectasis  
Chronic bronchopulmonary suppuration

#### ANATOMICAL DIAGNOSES

Bronchial adenoma  
Pulmonary atelectasis  
Bronchiectasis

#### PATHOLOGICAL DISCUSSION

DR TRACY B. MALLORY: It was possible to obtain the old microscopic sections of this patient, and on review of them it was clear to us that this was a so-called "adenoma." On that basis, Dr Edward D. Churchill decided to treat the case with a pneumonectomy. The resected lung showed a large, almost spherical tumor completely filling and absolutely plugging the bronchus to the lower lobe, and producing very marked bronchiectasis, with secondary atelectasis and fibrosis of the surrounding lung tissue (Fig 1). The tumor was large enough to have pressed on and occluded by external pressure the bronchioles running down to the lingula of the upper lobe. The lingula presented a more acute type of pneumonitis, a so

called "drowned-out" lung, without bronchiectasis. These peculiar bronchial tumors were first described as adenomas, which is perhaps not a good term, because they very rarely show any gland formation and an adenoma should be a tumor made up of tumor cells producing glands. The nature of this tumor is still uncertain. The tu-

and a variety of other tumors from time to time show bone-forming stroma. The bone in this case, as in all others that I have studied, seems to be a product of the stromal cells, not of the tumor cells.

X-ray studies of the tumor after its removal clearly showed the calcified bone in the tumor (Fig. 2),

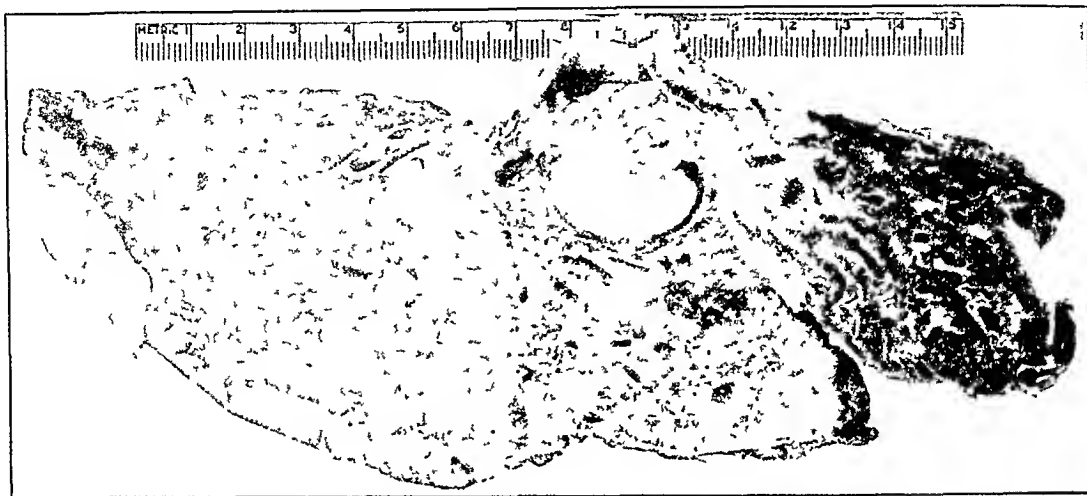


FIGURE 1. Photograph of Half of Resected Lung.

*Note the hemispherical adenoma filling the lower lobe bronchus, the dilatation of bronchi in the lower lobe (to the right of the tumor), with associated atelectasis, and the pneumonitis of the lingula of the upper lobe.*

mors are of very similar appearance, always made up of rather small uniform cells, never showing multinucleated giant cells, and never showing many mitotic figures. The cells are arranged in anastomosing cords or trabeculae, closely similar to so-called "carcinoid tumors" of the intestinal tract. They are not, however, argentaffin like the carcinoid tumors. A feature that has provoked a good deal of interest in recent years has been the finding in many of these tumors of trabeculae of bone. In this tumor, considerable amounts of bone were present.

The finding of bone in these tumors has led to the suggestion that they are mixed tumors. It has also been claimed that cartilage is sometimes found. I have not been impressed with cartilage as a component part of the tumor. They are slightly invasive tumors, and may surround the bronchial cartilages; consequently, the cartilage that one sees may be just an included remnant of the bronchocartilage. The bone might be a product of the tumor. It might also be a metaplastic reaction in the stroma of the tumor, such as we see from time to time in other tumors, but not with the frequency with which such a reaction is seen in this particular group. Fibroids of the uterus, cancers of the breast, adenomas of the thyroid gland

but I should not consider it possible to make it out on the chest plate.

DR. HAMPTON: I cannot see any bone in the area of the tumor. We have not demonstrated

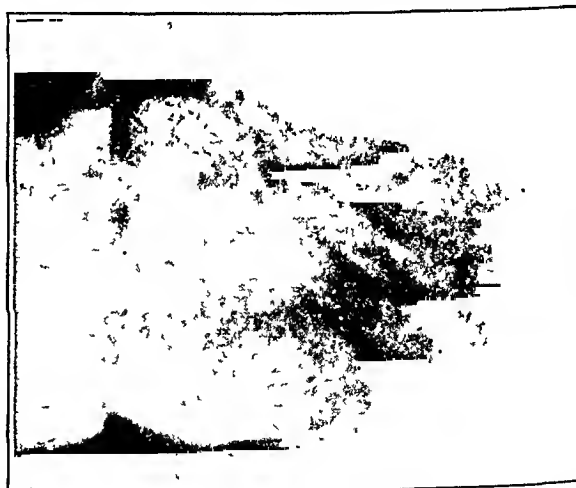


FIGURE 2. X-Ray of Resected Specimen Showing Ossification within the Tumor.

bone by x-ray study in these cases, perhaps because we have not tried hard enough.

DR. MALLORY: This had more than any of our other cases. Possibly, with an overexposed film, you might have been able to show it.

DR. HAMPTON: It is an important point for us.

## CASE 27512

## PRESENTATION OF CASE

A thirty seven year-old weaver was transferred from another hospital because of convulsive seizures for the previous two weeks.

About eighteen months before admission, while fishing, the patient fell and struck his head on the ice. He was unconscious for a very brief period and subsequently had a severe headache. He was in good health for the next six months and then began to lose weight, to be fatigued easily, and to vomit occasionally. After one of the attacks of vomiting, he complained of numbness and weakness on his right side. He had difficulty in forming sentences, and seemed to stumble over his words.

When first seen at the other hospital, eleven months before entry to this hospital, the patient was listless and apathetic. His pupils were equal and reacted normally. The fundi were not remarkable. The neck was slightly stiff. The right arm was completely flaccid, with absent reflexes. The right side of the face was flaccid, and the right leg was weak. Abdominal reflexes were decreased on the left, and absent on the right. The knee jerks were active, the right being greater than the left. The right plantar response was of Babinski type. The rectal temperature was 104.4°F. The blood showed a white cell count of 12,000. The blood Hinton reaction was negative. A roentgenogram of the skull showed a questionable area of increased density low in the left posterior parietal region. When lumbar puncture was performed, the initial pressure was too low to measure, and the fluid was cloudy and faintly xanthochromic. The gold sol curve was 050555000, and the Wassermann reaction was positive. There were 117 lymphocytes per cubic millimeter of fluid; the protein was 500 mg and the sugar 275 mg per 100 cc. Ten days after admission, the patient was discharged free of paralysis.

During the next three months, he received antisyphilitic therapy. Ten months after discharge, he had a bout of fever, associated with difficulty in talking, which cleared up in a few days. Several days later, an apparent convulsion was followed by persistent headache. A lumbar puncture gave bloody fluid under pressure. The following night, he had a severe convulsion and was readmitted to the other hospital.

At this time, the patient was restless and noisy. The temperature was 101°F, the pulse 100, and the respirations 40. The blood showed a white-cell count of 18,800 with 92 per cent polymorphonuclears, and a red-cell count of 4,500,000 with

75 per cent hemoglobin. The urine showed a heavy trace of albumin, with occasional red cells in the sediment. A lumbar puncture the next day yielded 25 cc. of bloody fluid under a pressure equivalent to 450 mm of water. After repeated convulsions, controlled with difficulty by sedation, the patient was transferred to this hospital for study.

The chest and abdomen were normal. The blood pressure was 110 systolic, 60 diastolic. Examination of the blood and urine showed no essential change. There were no motor weaknesses, and no sensory deficiencies, except for impairment of position sense in the left toes. The neck was stiff, and there were positive Kernig reactions. The tendon reflexes were equal and active, with normal plantar responses. The fundi were normal. The speech was hesitant, and there was some loss of recent memory. The attention wandered.

A roentgenogram of the skull showed questionable erosion of the posterior clinoid processes. The shape and size of the sella were normal, and the convolutional markings were of normal prominence. Several apparent intradural areas of calcification lay on either side of the midline, in the frontal region. A roentgenogram of the chest showed no significant changes.

On the third hospital day, two convulsive seizures occurred, preceded by a bout of projectile vomiting. During the second period of convulsions, the patient lay on his right side, his eyes deviating to the extreme right. Half an hour later, there were bilateral, Babinski plantar responses and an almost inexhaustible left-ankle clonus. The pupils were constricted, and the eyes turned toward the left. Respirations were stertorous. After this second seizure, the patient never regained consciousness. A lumbar puncture shortly before death demonstrated grossly bloody fluid, with a pressure of over 200 mm; the gold sol curve was 4453433310, the protein 206 mg. per 100 cc, and the Wassermann reaction negative. Death occurred on the fourth hospital day.

## DIFFERENTIAL DIAGNOSIS

DR. G. COLLET CANER. After reading the whole history, I think it is clear that the head injury which the patient sustained eighteen months before entry to this hospital was not a factor in the case. The physician who took care of the patient when he first entered the other hospital might have had some difficulty in ruling out subdural hematoma as a cause of the symptoms. However, I think it could have been ruled out even at that time. This patient did not have any headache, and a subdural hematoma almost always causes

headache. With a subdural hematoma sufficiently large to cause a hemiplegia, one would certainly expect headache. One would also expect an increase in spinal-fluid pressure, as well as drowsiness or coma, which the patient did not show. The history of the onset of the patient's illness, characterized by loss of weight, rapid fatigability and vomiting, do not suggest a subdural hematoma, which is also made unlikely by the fact that the paralysis of the left arm was flaccid, with absent reflexes. A paralysis caused by a subdural hematoma should be spastic from the beginning. When a palsy due to involvement of the corticospinal motor tract in the brain is of the flaccid type, one expects the lesion causing it to be recent and of sudden onset, as with either hemorrhage or embolism. There were therefore numerous reasons at the time of the first entry for thinking that the numbness and weakness were not due to a subdural hematoma, and there was a strong indication that they were caused by a vascular accident, such as hemorrhage.

If the patient had had a vascular accident at that time, we are interested in its cause. One possibility is hemorrhage into a tumor or in the vicinity of a tumor. The spinal-fluid findings, except for the low pressure and the low sugar, might be explained by brain tumor. The x-ray at that time indicated an area of increased density, low in the left posterior parietal region, which suggests the possibility of meningioma, but one would not expect a meningioma to be associated with hemorrhage. I think that hemorrhage in the region of a tumor could not have been excluded with certainty at the time of the first entry on the basis of the information here given, but the subsequent history is very much against brain tumor, and I think we can now safely rule it out as the cause of the presumed vascular accident.

The usual cause of a vascular accident in a patient of this age, without hypertension, is vascular syphilis. The blood Hinton reaction should be a better criterion of vascular syphilis than the spinal-fluid Wassermann reaction, and the blood Hinton reaction was negative. The positive spinal-fluid Wassermann reaction was obtained on a fluid that was xanthochromic and had a high total protein, and fluids of this character not infrequently give a false-positive Wassermann reaction. The spinal-fluid findings suggest the possibility of a syphilitic meningitis, but certain features are not consistent with this diagnosis. A syphilitic meningitis sufficiently acute to cause only 117 lymphocytes in the lumbar fluid should not cause a total protein much above 50 or 100 mg. instead of one of 500 mg. per 100 cc. Likewise,

any meningitis sufficiently acute to cause such a high total protein should also give a high pressure. The low spinal-fluid sugar is also strongly against a syphilitic meningitis. I therefore believe that the spinal-fluid findings do not favor syphilis and that even at the first entry a diagnosis of syphilis should not have been made on the basis of these findings. The latter part of the history is too malignant for syphilis. I feel safe in ruling it out.

The low spinal-fluid sugar and the high protein suggest a tuberculous meningitis, but the low pressure is strongly against it. The patient also would have appeared sicker if he had had a tuberculous meningitis. The rapid recovery and the long remission of course rule out this diagnosis.

One wonders whether the spinal-fluid pressure might actually have been high in spite of the findings in lumbar puncture. If one does not use a manometer to measure the pressure, one may think that the pressure is low if the fluid drops out slowly, which may happen with a high pressure if the lumen of the needle is partially obstructed. If, however, a manometer is used, the fluid will rise slowly in the manometer and will indicate the true pressure, even though the needle is partially obstructed. The statement that the pressure was too low to be measured indicates that a manometer was used, and we must therefore accept the statement that the pressure actually was low.

It seems to me that the spinal-fluid findings can best be explained by subarachnoid bleeding. The chief objections are the low spinal-fluid pressure and the low sugar. A subarachnoid hemorrhage sufficiently large to cause hemiplegia should give an increased pressure. I think, however, that the low pressure may be explained on the supposition, suggested by the phrase "when lumbar puncture was done," that the lumbar puncture was not done at the time of admission to the hospital, but was done just prior to discharge; if that were so, the subarachnoid bleeding would have occurred ten days or more before lumbar puncture—sufficient time for blood cells to disappear from the fluid and for the fluid to become xanthochromic. It is possible that the total protein might still have been high ten days after the hemorrhage occurred, as a result of the serum that got into the fluid at that time. Subarachnoid hemorrhage would explain the stiff neck, but it would not explain the low sugar very well. Although it is stated in the literature that a low spinal-fluid sugar may be caused by hemorrhage into the subarachnoid space, I do not believe that we have seen it here,—at

least I have not. We expect the spinal-fluid sugar to be normal in these cases. I cannot explain the low sugar in this case, unless it is an error; I cannot use it in the differential diagnosis, and think that we must disregard it. The rectal temperature of 104.4°F., although high, seems best explained by subarachnoid hemorrhage; there is nothing to indicate affection of hypothalamic centers.

If the cause of the aphasia and flaccid paralysis was subarachnoid bleeding, what caused it? A very frequent cause is a small congenital saccular aneurysm. Leakage from such an aneurysm located on the ascending frontal branch of the middle cerebral artery might have caused the signs shown by the patient, and an aneurysm in that vicinity might have been open to surgical treatment. It seems to me that this possibility was sufficient to have warranted surgical intervention.

The patient apparently was quite well for ten months after discharge, and then he had an attack of aphasia associated with a bout of fever. One might explain this by a recurrence of subarachnoid bleeding. Again, the bout of fever is hard to explain, but might be explained on the same basis on which we explained it before. The aphasia might have been caused by a thrombosis, but this would not cause fever. Multiple sclerosis may cause transitory symptoms and a slight rise in temperature, but there is nothing in favor of multiple sclerosis in the rest of the record.

Several days later, the patient had a convulsion followed by a persistent headache, and lumbar puncture then gave a bloody fluid. The bloody fluid is definite evidence of bleeding into the subarachnoid space, and the convulsions can be explained as the result of the cortical irritation caused by the blood. The findings on admission to the other hospital were consistent with subarachnoid hemorrhage, except for the urinary examination, which showed a heavy trace of albumin, with occasional red blood cells. I should not expect a subarachnoid hemorrhage to cause these findings. They suggest the possibility of a bacterial endocarditis, but the rest of the record does not make this at all likely, and I think we can rule this out.

On admission to this hospital, the patient showed findings characteristic of meningeal irritation presumably due to subarachnoid hemorrhage. Since he was not unconscious, he probably did not have a very large hemorrhage at this time and the earlier hemorrhages were also probably not large.

X-ray films in this hospital showed a question of erosion in both posterior clinoid processes and some areas of calcification that do not seem par-

ticularly significant; I should like to see the films, however.

DR. JAMES R. LINGLEY: I think that the erosion of the posterior clinoid processes is questionable. There is no decalcification of the processes, the sella turcica is normal in size, and there is no evidence of destruction; therefore, I think we can probably dismiss that as of no importance. The bones of the vault are rather heavy and dense, but I do not see any definite evidence of hyperostosis to go with a diagnosis of meningioma. The areas of calcification are best seen in the antero-posterior view. They are not linear, as one would expect in an angioma. They are rather flat, and in the lateral view I think you can see that they lie anteriorly. They are probably in the dura and therefore are of no importance. The skull shows no evidence of chronic pressure, and the examination is essentially negative.

DR. CANER: On the third hospital day, the patient had two convulsions preceded by a bout of projectile vomiting, and showed grossly bloody spinal fluid under increased pressure. Evidently, he had had another subarachnoid hemorrhage, which was acute and large. The eyes were turned first to the right and then to the left. That indicates irritation, followed by paralysis of the center for conjugate deviation at the base of the second left frontal convolution, or of the fibers connecting this center with the nucleus of the sixth nerve on the opposite side of the pons. The persistent clonus on the left suggests a lesion on the right. However, there is good evidence that the patient previously had had vascular accidents on the left because of an aphasic attack and because of an attack of flaccid paralysis of the right arm and face associated with aphasia. I should like to explain the last hemorrhage by the same lesion that caused the earlier hemorrhages, although saccular aneurysms are frequently multiple. I do not believe that we can do much more than guess where this last hemorrhage started, but I am fairly confident that it ruptured into the ventricles, as indicated by the small pupils, bilateral Babinski responses, unconsciousness and rapid death.

The assumption that bleeding from saccular aneurysms was responsible for the repeated vascular accidents does not explain some things in the history. It does not explain the red cells and the albumin in the urine or the symptoms at the beginning of the illness, but other common causes for repeated vascular accidents seem unlikely. I have already given reasons why I think syphilis is unlikely. Arteriosclerosis also seems improbable in a man of this age without hypertension. Peri-

arteritis nodosa may cause all the findings recorded in the history. It may cause loss of weight, fatigability and vomiting, symptoms that the patient had at the onset of the illness and are otherwise unexplained. However, very few cases have been reported of repeated attacks of cerebral hemorrhage resulting from periarteritis nodosa. It seems to me that this diagnosis is much less likely to be the true one, even though it would explain the whole case. I therefore conclude that the autopsy will show that this patient died because of a subarachnoid hemorrhage that ruptured into the ventricles and was caused by rupture of a saccular aneurysm. It is my guess that the ruptured aneurysm will be found on the ascending right frontal branch of the middle cerebral artery.

DR. JAMES B. AYER: I know the case, but should like to comment on one statement made by Dr. Caner with which I disagree—that is, that we should pay no attention to the low spinal-fluid sugar. Our laboratory is accurate on this test. Sugar of this amount, 27 mg. per 100 cc., is almost always indicative, or at least suggestive, of infection somewhere in or near the fluid pathways.

DR. CANER: I should agree ordinarily, but this report came from another laboratory. Certainly, I cannot fit the low sugar into my diagnosis.

DR. AYER: Assuming that the other laboratory is correct, I believe we ought to think of infection.

#### CLINICAL DIAGNOSES

Spontaneous subarachnoid hemorrhage.  
Cerebrovascular syphilis.

#### DR. CANER'S DIAGNOSES

Congenital saccular aneurysm.  
Subarachnoid hemorrhage.  
Rupture into the cerebral ventricles.

#### ANATOMICAL DIAGNOSES

Ruptured aneurysm of circle of Willis, with subarachnoid and intracerebral hemorrhage.  
Arteriosclerosis of coronary arteries (slight) and of aorta (slight).  
Retention cyst, right kidney.

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: The significant findings were limited to the head. There was slight generalized arteriosclerosis. The kidneys were perfectly normal. I have no explanation for the albuminuria.

DR. CHARLES S. KUBIK: In some cases of spontaneous subarachnoid hemorrhage, there is an albuminuria, which apparently is not due to any serious kidney disease and which rapidly subsides if the patient recovers. In this case, there was a small aneurysm, about 4 mm. in diameter, in the angle between the right anterior cerebral and anterior communicating arteries. The aneurysm itself was surrounded by a fair amount of old brownish blood clot in which there was some blood pigment indicating that there had been previous bleeding. It had finally ruptured, and the resulting hemorrhage broke through the pia into the left frontal lobe and from there into the anterior horn of the left lateral ventricle. I think it is rather difficult even now to explain the severe right hemiplegia and aphasia that occurred with the first episode, because if there had been a hemorrhage into the left frontal lobe at that time, one would not have expected such a quick recovery. There were no other aneurysms. Although sections of the aneurysm are not yet available, one can be reasonably certain that this is a so-called "congenital aneurysm" and that syphilis can be excluded as an etiologic factor.



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## PEACE ON EARTH . . .

IN this critical year of 1941, with still more critical years ahead, we come again to the observance of Christmas, the day of peace on earth, coming so soon after the day of thanksgiving and after the day on which we commemorate the armistice of 1918. The latter was the date to be annually remembered and to be revered in perpetuity, on which warring nations laid down their arms and peace came to brood forever over a world that had learned the futility of force. It was, unfortunately, fittingly titled, for its name suggests the essence of impermanence—according to Noah Webster, a “brief suspension of hostilities by agreement.”

Civilization's great error, certainly of our generation, has been to think of peace as a natural

condition—as the normal state of affairs that immediately succeeds any misunderstanding that may occur in the relations between man and man and between nation and nation. Unfortunately, peace is not like the air (once free) around and above us, which abhors a vacuum and forces it out of existence, or like the waters of the sea (whose freedom was once guaranteed by mutual understanding), which seek and maintain their constant level.

Following the “brief suspension of hostilities” were days of unreality, when the Christian nations, exhausted by a detested, even if triumphant, contest, believed that at last a state of permanent peace had been achieved—a state to be maintained in the council chamber and by Omnipotent guidance, and by little else. We have been awakened from that dream, and our fool's paradise has disappeared. We have come back to the wholesome, if bitter, reality of existence, and an appreciation of the fact that human nature does not change overnight or in a generation—perhaps not in any known period, even as it can be reckoned astronomically. Peace may remain the goal of our ambitions, but it is a higher goal, because we know now that it represents a positive virtue and not a passive state.

Peace is the final objective of our current endeavor; but it must be attained by aggressive action, it must be cultivated and consolidated and fostered, and it must be constantly defended by force—forever, so far as our present minds can reach. When this objective is attained, then can we truly say that, because of our determination to have it so, there may be peace on earth, *to men of good will*.

## PROCUREMENT AND ASSIGNMENT SERVICE

ONE of the greatest problems facing the Government is the procurement of physicians for and their assignment to various governmental positions. Owing to the declaration of war, the demands for medical officers by the United States Army, Navy and Public Health Service will be enormously increased; furthermore, many physicians are needed

by the United States Civil Service Commission and Veterans' Bureau. Industrial and civilian needs, however, should not be neglected, and recent graduates from medical schools should be permitted to continue their educational programs, which demand a minimum of one year of hospital training and at least three or four years for those who are to qualify properly as specialists. The Committee on Medical Preparedness of the American Medical Association anticipated this situation, and on the recommendation of the committee, the House of Delegates passed a resolution last June, which urged the establishment of a governmental agency for the procurement and assignment of physicians.

On October 31, President Roosevelt authorized the Procurement and Assignment Service, a subdivision of the Office of Defense, Health and Welfare Services, Federal Security Agency, under the direction of Administrator Paul V. McNutt. The functions of this service are as follows: to receive from various governmental and other agencies requests for medical, dental and veterinary personnel, to secure and maintain lists of available personnel that show detailed qualifications and to utilize all suitable means to stimulate voluntary enrollment, with due regard for the over-all public-health needs of the Nation, including those of governmental agencies and civilian institutions. According to a suggestion contained in the resolution of the House of Delegates, the board is composed of representatives of the civilian medical profession, as follows: Dr. F. H. Lahey, of Boston, chairman; Dr. H. S. Diehl, of Minneapolis; Dr. J. E. Paullin, of Atlanta; Dr. H. B. Stone, of Baltimore; and Dr. C. W. Camalier, of Washington, D. C., a past president of the American Dental Association. The board has been organized, and at its initial meeting the following subcommittees were appointed: Medical Education, Hospitals, Public Health, Women Physicians, Information, Industrial Health and Medicine, Dentists, Veterinary Medicine and Negro Health.

Although the state of war will undoubtedly result in additional functions and increased responsibility, the wisdom of the appointment of a board of this sort and for this purpose cannot be denied,

and it is hoped that many of the unfortunate orders and recommendations that led to the improper placement of physicians in the services and to unwarranted shortages of physicians in certain areas of the United States during World War I will be avoided.

## MEDICAL EPONYM

### LITTLE'S DISEASE

William John Little (1810-1894) wrote "On the Influence of Abnormal Parturition, Difficult Labours, Premature Birth and Asphyxia Neonatorum on the Mental and Physical Condition of the Child, Especially in Relation to Deformities" in the *Transactions of the Obstetrical Society of London* (3: 293-344, 1862).

Asphyxia neonatorum, through resulting injury to nervous centres, is the cause of the commonest contractions which originate at the moment of birth, namely, more or less general spastic rigidity, and sometimes of paralytic contraction.

The former class of affections may be described as impairment of volition, with tonic rigidity and ultimately structural shortening, in varying degrees, of a few of many of the muscles of the body. Both lower extremities are more or less generally involved. . . . Sometimes the affection of one limb only is observed by the parent, but examination usually shows a smaller degree of affection in the limb supposed to be sound. The contraction in the hips, knees, and ankles, is often considerable. The flexors and adductors of thighs, the flexors of knees, and the gastrocnemii, preponderate. In most cases, after a time, owing to structural shortening of the muscles and of the articular surfaces, the thighs cannot be completely abducted or extended, the knees cannot be straightened, nor can the heels be properly applied to the ground. The upper extremities are sometimes held down by preponderating action of pectorals, teres major and teres minor, and latissimus dorsi; the elbows are semi-flexed, the wrists partially flexed, pronated, and the fingers incapable of perfect voluntary direction.

R. W. B.

## OBITUARY

### LUCIA FLORENCE VICKERY

1860-1941

Dr. Lucia Vickery, a pioneer among women in medicine, died at her home, 37 Greenough Avenue, Jamaica Plain, Massachusetts, on October 23, in her eighty-second year.

Born in Portland, Maine, on April 26, 1860, she received her early education at St. Catherine's Hall at Augusta, Maine. She then studied voice and piano for two years at the New England Conservatory of Music. Deciding to become a nurse, she trained at the Boston City Hospital. After graduating from the hospital, she told the super-

intendent, Dr. Rowe, that she wished to become a physician. When he said, 'Why spoil a good nurse by becoming a poor physician?' she answered, 'I am not going to be a poor physician.'

In 1888, she entered the Woman's Medical College in the New York Infirmary, from which she graduated in May, 1892. In the summer of 1891, she went abroad, visiting hospitals in France and Germany. She interned at the New England Hospital for Women and Children, and then started private practice in Jamaica Plain, in which she was actively engaged for nearly fifty years. In her chosen field of general practice, her contribution was outstanding, and among patients and friends alike, she will be sadly missed. For the past few years, she had maintained a convalescent home, bringing to this later work the same rare success that characterized her general practice. She was a member of the Massachusetts Medical Society, and for several years was elected to the Council.

Among her fellow physicians, her life and work were a constant inspiration. She was strong and kindly in nature, having a forceful personality combined with rare judgment and understanding. Those who knew her intimately found her always cheerful, even in her last illness, with wonderful courage and fortitude. Those who have had the privilege of knowing her well will greatly miss Dr. Vickery.

K S S

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

#### FATAL HEMORRHAGE FOLLOWING INTERNAL PODALIC VERSION

A thirty six year old para III had been followed inadequately after the fifth month of pregnancy. She entered the hospital at term and in labor. There was some vaginal bleeding.

Physical examination was negative, and the past medical history was irrelevant. The blood pressure was normal. The uterus was at term. It is stated that hemorrhage during labor, although not severe, was constant. Because labor was ineffectual, the cervix was dilated manually, and an internal podalic version was performed, with the delivery of a stillborn child. There was profuse post partum hemorrhage, from which the patient did not rally. She died while preparations for transfusion were being made.

\*A series of recorded case histories by members of the section will be published weekly. Conventions and lectures by specialists are solicited and will be discussed by members of the section. Lectures should be addressed to Dr. Raymond A. T. U. S. Sec'y, 330 D. M. St., Boston.

**Comment.** From the evidence at hand, there is little to praise in the obstetric treatment given to this patient. Because of a moderate, constant hemorrhage, with ineffectual labor, the cervix was dilated and internal podalic version performed. It is probable that this multipara had a low attached placenta, possibly a marginal previa. In that event, rupture of the membranes, possibly with the insertion of a Voorhees bag, and the use of small doses of pituitary extract would have effected full dilatation of this cervix without further loss of blood, and normal delivery might have followed.

**Accouchement force**, which was probably performed, is an operation of historic interest and has no place whatever in modern obstetrics; it is very likely that the tremendous hemorrhage that followed delivery was caused by rupture of the lower segment of the uterus. Such a procedure cannot be condoned, and is not tolerated in hospitals whose obstetric services are properly supervised. The trustees' responsibility for such disasters has been brought out in this column before they are accountable for good or bad obstetrics and until proper supervision is demanded in all institutions where obstetrics is practised, an occasional case of ill advised operating will result in such a fatality.

### DEATHS

**BLAKE**—ALLEN H. BLAKE, M.D. of Somerville died December 9. He was in his sixty first year.

Born in Cambridge. Dr. Blake received his degree from Harvard Medical School in 1904. He joined the staff of the Somerville Hospital in 1910, and served there until his death. He was a former president of the Somerville Medical Society and of the Middlesex South District Medical Society, and was a member of the Radiological Society of North America. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

He is survived by his widow.

**SAWYER**—WALTER F. SAWYER, M.D. of Fitchburg died December 9. He was in his seventy fourth year.

A native of Keene, New Hampshire. Dr. Sawyer received his degree from Harvard Medical School in 1893. He was a fellow of the American College of Surgeons and a former president of the Worcester North District Medical Society. He was a member of the Massachusetts Medical Society and the American Medical Association.

He is survived by his widow, a son and daughter and four grandchildren.

## NEW HAMPSHIRE MEDICAL SOCIETY

### DEATH

**POTVIN**—VICTOR E. POTVIN, M.D. of Claremont died December 10. He was in his fifty seventh year.

A native of Southbridge, Massachusetts. Dr. Potvin received his degree from the University of Montreal Faculty

of Medicine in 1909. He was a member of the New Hampshire Medical Society and the American Medical Association.

He is survived by his widow, two daughters and three brothers.

## DEFENSE ACTIVITIES

### CIVILIAN DEFENSE

#### DUTIES OF THE LOCAL CHIEF OF EMERGENCY MEDICAL SERVICE

#### Medical Division Memorandum No. 3, Office of Civilian Defense

In order to expedite the organization of the emergency medical services and provide for their effective administration, it is important that each local civilian defense council appoint without delay a local chief of emergency medical service. He should be an outstanding medical leader and should be selected in consultation with the state defense council, the local medical society and the local health officer. To facilitate the integration of all local medical resources into a comprehensive program for civilian protection, the local chief of emergency medical service should be assisted by a medical advisory council, consisting of the local health officer, an experienced hospital executive and representatives of the local medical society, the local nursing profession, the American Red Cross and any participating voluntary agencies.

Under the administrative authority of the local director of civilian defense the duties of the local chief of emergency medical service are:

(1) To determine the scope of the activities of all official and voluntary organizations which are to participate in the emergency medical program of civilian defense, to integrate these organizations into the comprehensive local program and to assist them in expanding their activities to the limit of their resources in personnel and equipment.

(2) To assist hospitals in the locality to organize, equip and train emergency medical field units, as outlined in Medical Division Bulletin No. 1, *Emergency Medical Service for Civilian Defense*.

(3) To inspect and select sites for the establishment of casualty stations.

(4) To make a spot map of the locality, indicating the locations of hospitals, appropriate sites for casualty stations, depots for storage of stretchers, blankets and collapsible cots, and the locations of rescue squads. The map should indicate the number of emergency medical squads in each hospital. Copies of the map should be supplied to control centers, police and fire departments, health department, local Red Cross chapter, state defense council, regional director, regional medical officer and all co-operating hospitals.

(5) To plan and establish adequate transportation service for casualties and medical personnel in consultation with local governmental departments, American Red Cross and voluntary agencies.

(6) To arrange with the local control authority for field drills of emergency medical units and rescue squads in collaboration with police and fire auxiliaries, disaster relief and canteen services of the American Red Cross, ambulance transport service and other civilian defense units, and to supervise such drills.

(7) To make an inventory of hospital beds in the locality and of the possibilities for emergency expansion in bed capacity.

(8) To assist the authorities charged with preparing plans for evacuation in making an inventory of hospitals, convalescent homes, sanatoriums, hotels and other structures within a radius of 50 to 100 miles, which might be used as base hospitals to which patients in city institutions could be evacuated.

(9) To assist the local central volunteer bureau in establishing courses for volunteers in the field of health, medical care, nursing and related activities.

(10) To stimulate recruitment of volunteers for nurses'-aide courses of the American Red Cross, assist the local Red Cross chapter in establishing training centers for volunteer nurses' aides at appropriate hospitals and assist the Red Cross placement bureau in placing nurses' aides with hospitals, clinics, health departments and field nursing services after completion of training.

(11) To stimulate and guide extension of first-aid training courses as widely as possible among the local population through the American Red Cross and other official and voluntary agencies.

(12) To stimulate and guide industrial plants, business establishments and governmental bureaus in the locality in the training and organization of effective first-aid detachments among the employees.

(13) To collaborate with state and local health departments and through them with the regional sanitary engineer in a comprehensive program for the protection of the community against emergency sanitation hazards.

(14) To collaborate with local and state defense councils, Office of Civilian Defense, Federal Security Agency, Children's Bureau and other local, state and federal authorities in the preparation of plans for evacuation, with particular attention to the medical needs of the population under such circumstances.

(15) To keep the community and particularly the members of the health and medical professions and the participating official and voluntary organizations informed of the plans and activities of the local emergency medical service.

## BOOK REVIEW

*That None Should Die.* By Frank G. Slaughter, M.D. 8°, cloth, 423 pp. New York: Doubleday, Doran and Company, Incorporated, 1941. \$2.75.

This is a medical novel written by a physician in active practice. Its action, at least up to a point, is obviously based on personal experience, and the picture of student life and practice, both hospital and private, is reasonable enough. But the author attempts to project just what practice will be under governmental control, of which, with all due respect, neither he nor anyone else can be sure, although each person may have his fears. One is not much interested in stories that take a flier into the future, and as a story pure and simple, — which a conventional novel really ought to be, — this is not a particularly thrilling piece of work.

(Continued on page x)

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## THE CARDIOVASCULAR EXAMINATION OF THE ARMY RECRUIT\*

HENRY JACKSON, JR., M.D.†

BOSTON

IT is obvious to anyone who has followed the course of the present war that a high degree of stamina is vital to the modern soldier, perhaps even more so than ever before. It is necessary, therefore, to adhere to the strictest standards when deciding whether or not a man should be classified as "fit for general military service." In reaching a conclusion, one must visualize as nearly as one may from this present distance the rigors of modern warfare, and furthermore, the examiner must bear in mind the question of possible future compensation arising from a certificate of disability discharge.

Criteria that might rightly be applied to civilian life may not be proper for the modern military regime, and it should be constantly remembered that the army of today functions more than ever as a unit and that even the temporary disability of one man may be of grave import to the unit as a whole. Moreover, it is probably incorrect to assume that because a man has been "athletic" in civil life he will necessarily be able to endure the hardships of an extended and concentrated campaign under modern conditions. One professional athlete who had successfully participated in his chosen vocation in October, 1940, was properly rejected by the United States Army for gross physical defects a month later. In this respect, Paragraph 1-b in A. R. (Army Regulations) 40-105 is worth recalling: candidates for commissions in the organized reserves "must be free from any defect or pathological condition which would interfere with the performance of the duty expected of them in the Army, or which would, as a result of service, be especially liable to undergo progressive change or to become the basis for a claim against the Government in the event of call to active service."

This communication is concerned only with the cardiovascular system of the recruit, and much has been learned in this respect in the past twenty-five years. The standards relative to other body systems should be quite as exacting.

Up to May, 1918, "heart disease" ranked third in the list of causes of discharge from the British Army and the Royal Navy,<sup>1</sup> yet in 1938, diseases of the circulatory system accounted for but one tenth of the annual death rate in the United States Army.<sup>1</sup> It is problematical whether this major difference is due to increased attention to the cardiovascular system, to the reduction of the incidence in certain diseases leading to cardiovascular disorders or to the fact that from 1914 to 1918 the British forces were actually at war. It is likely that all these factors are involved. On the other hand, it is interesting that only 0.8 per cent of 37,000 men at Camp Devens up to May, 1918, were rejected for cardiovascular disorders,<sup>2</sup> and that during World War I approximately 0.5 per cent of all men drafted and sent to military camps were rejected for cardiovascular defects.<sup>3</sup> It should be especially noted that neither of these statistical analyses includes those men rejected by their local draft boards. The figures cited correspond more closely to those of the present induction centers (now designated as examining centers). The Metropolitan Life Insurance Company rejects as "ineligible for standard life insurance" approximately 2 per cent of all applicants below the age of thirty-five. Preliminary figures show that, in the past year, slightly over 3 per cent of all men have been rejected for cardiovascular disease by their local examining boards.<sup>4, 5</sup>

The various induction centers of the United States Army are guided in their selection of men by regulations covered in M. R. (Mobilization Regulations) 1-9. At these centers, only men are examined who have been passed as physically fit for general military service by their local selec-

\*From the Thorndike Memorial Laboratory, and the Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School.

†Chief civilian internist, Boston Induction Center, Fourth Recruiting Area; assistant professor of medicine, Harvard Medical School.

tive-service boards, together with those men applying for regular enlistment in the Army and a certain number of aviation cadets who have been, or will be, examined further by a flight surgeon.

Under Paragraph 55 of M. R. 1-9, it is apparent that to be placed without question in Class 1-A (general and unlimited military service) a man must have a cardiovascular apparatus free of all but the most trivial deviations from the strict normal. The apex impulse must be within the midclavicular line, and no thrills or "important murmurs" may be present. The pulse rate must be under 100 and over 50. No cardiac arrhythmias are allowed other than sinus inequality and infrequent extrasystoles. More than transitory hypertension patently due to excitement is disqualifying. Neurocirculatory asthenia, unless mild, is likewise a cause for rejection. All this is as it should be, and it must be especially noted that, at present, the induction centers—in contrast to the local examining boards—either flatly accept or reject a man. The Army does not now consider Class 1-B (limited service), except under very special circumstances requiring a waiver from the War Department. In this respect, the induction centers differ from the local examining and advisory boards, which may, at their discretion, place a man in Class 1-A, 1-B or 4.

However, according to the same regulations, it is incumbent on examining physicians to accept for service men with "accidental functional murmurs" or with other findings that do not indicate disease or impair the selectee's ability to undergo severe bodily exertion, and to exclude those with defects, however innocent, appearing at the time of examination that would interfere with their activities (Paragraph 60, M. R. 1-9).

As a result of the experience of eleven months at the Boston Induction Center, Fourth Recruiting Area, and with the help of several cardiovascular experts, certain conclusions—subject to subsequent change—have been drawn. It seems worth while to bring these conclusions to general attention for future reference and, perhaps, amendment.

~ \* \*

It is obvious that all recruits with organic heart disease of whatever nature should be summarily rejected (Paragraph 57, M. R. 1-9).

No recruit should be accepted if he has a diastolic murmur at either the apex or the base.

It is probably best that all recruits having an undoubted history of rheumatic fever should be rejected, even if there is no demonstrable cardiac damage at the time of examination. The possibility of recurrent rheumatic disease and of late development of valvular or myocardial disease

must be considered. It is obvious that certain men may wittingly and with malice aforethought feign such a history. In such cases, documentary evidence from the patient's physician or hospital records is of the greatest value. On the other hand, men may knowingly conceal their past disease, although there are severe penalties for so doing. In such cases, a history of repeated nosebleeds, continued unexplained fever or chorea (infrequently associated by recruits with rheumatic fever) may be of some help. Recently, a man was accepted by the internist only to be rejected by the neurologist, who elicited an unquestionable past history of chorea of many weeks' duration. In doubtful cases, an electrocardiogram and six-foot film of the heart should be taken before final acceptance or rejection.

All applicants showing arteriosclerosis or arteriolar sclerosis should be rejected.

Any gross inequality of the pulse should be a cause of rejection. It is commonly taught that excitement, sleeplessness, alcoholic excesses and the like predispose to extrasystoles, yet I have been surprised to find how rare this irregularity is in recruits or selectees, even though many of them have been subjected to one or all of the supposed inciting causes. This paradoxical experience should serve to emphasize the importance of any notable arrhythmia.

The question of the significance of systolic murmurs is as difficult at induction centers as in civil life. It seems reasonable that the presence of a low-pitched, soft, systolic murmur localized at the pulmonary-valve area, or even heard at the apex, unaccompanied by other cardiac abnormalities and not preceded by a history of rheumatic fever or chorea, may be regarded as of no consequence, especially if the man appears otherwise healthy and robust. A mitral systolic murmur accompanied by an increased pulmonic second sound, slight cardiac enlargement and a history of rheumatic fever is, on the other hand, obviously a cause for rejection. Between these two extremes lie many cases. There are competent cardiologists who believe that a systolic murmur at the apex, even though loud and transmitted to the axilla, if unaccompanied by other signs should be regarded as consistent with good health. This may well be true in civil life; it is probably not true in war, and there is some evidence that even in civil life such a murmur cannot be dismissed too lightly.<sup>6,7</sup> In this respect, the opinions of Bourne<sup>8</sup> are of interest. Discussing the examinations of the heart in British recruits, this author says: "If a systolic murmur is entirely absent in the erect position, it is unlikely to be organic. If

present only in the erect position, it is almost certainly functional in type. If absent during phases of respiration, it is unlikely to be organic." Essentially the same views are expressed by Parkinson.<sup>1</sup> It is undoubtedly wise to reject any man who shows a loud, harsh, systolic murmur transmitted to the axilla *even though such a murmur is unaccompanied by other pathologic signs*. That this dictum is contrary to the teachings of some is fully recognized. The opinion has not been hastily formed.

Mitral 'presystolic' murmurs are also difficult to appraise. The truly presystolic murmur—especially if of the rough, crescendo type, accompanied by a loud snapping first sound and increased by exercise—should be regarded as a cause for rejection. In many cases, however, a selectee or recruit may come to the induction center with a pronounced tachycardia, and in these men one not infrequently hears what seems to be a presystolic murmur. It is in actuality more a grating quality to the first sound in an overactive heart, and it almost always disappears if the man lies down for half an hour. Such a murmur may be disregarded if no other abnormalities are present and if the past history is negative.

Men with pulse rates of 100 or over should be rejected unless the tachycardia subsides with adequate rest. It is essential to distinguish between the tachycardia caused by an unstable and nervous temperament and that transiently due to excitement, temporary nervousness or lack of sleep. The latter type will almost invariably subside after half an hour's or an hour's recumbency with the added distraction of watching others undergo their examinations. It is obvious that acute infections may similarly be accompanied by tachycardia, usually, the site and nature of the infection can easily be found. Tachycardia that does not subside during the day of examination should probably be regarded as evidence of an unstable cardiovascular or nervous system and should therefore be considered a cause for rejection: a man on active service can scarcely demand a "few days' rest." If the tachycardia is the only abnormality, the examiner may be justified, in rare cases, in asking the man to return on another day for a second examination. Initial rates of 130 or over very seldom come down to normal. Marked tachycardia may follow the use of certain drugs either for therapeutic purposes or because the man being examined is a malingerer. This possibility should always be borne in mind, although not many such cases have been recognized at the Boston Induction Center.

The question of blood pressure is a most difficult one. The regulations (M R 19) state that men should be rejected who have a "persistent blood pressure at rest above 150 millimeters systolic or above 90 diastolic, unless in the opinion of the medical examiner the increased blood pressure is due to psychic reaction and not secondary to renal or other systemic disease." When the first inductions took place in Boston in November, 1940, it was the opinion of one cardiovascular expert that, for all practical purposes, blood-pressure readings could be dispensed with, since the number of true hypertensive patients in this age group would be negligible. This view has gradually been modified, and blood pressures are now taken on all men with initial pulse rates of over 100, on all men showing more than a slightest possible trace of albumin and on all obese applicants. If the blood pressure is more than 150 systolic or 90 diastolic, the recruit is rested until either the pressures have become normal or it is apparent that they will remain elevated during the day of examination. The original practice of having men return on subsequent days for further check-ups has been discarded. If rest for three days is needed to attain normal readings, it is probable that the applicant has either essential high blood pressure or neurocirculatory asthenia. In this area, we have not, so far as we are aware, encountered blood pressures elevated because of drug addiction. In other parts of the country, such falsely elevated blood pressures are not uncommon. The possibility of malingering should always be borne in mind. Adopting a long range and conservative view, and influenced by the work of Hines,<sup>10</sup> we now reject men whose systolic blood pressures remain over 150 and whose diastolic pressures remain over 90 during the day of examination. Grossly elevated blood pressures frequently fall to strictly normal limits within an hour. Such variations from the normal may probably be disregarded.

Neurocirculatory asthenia is, according to Bourne,<sup>11</sup> the "commonest cause of cardiovascular breakdown under the strain of active service." The subjects are usually high strung, repressed, fastidious in their habits and subject to palpitation, precordial distress, abnormal sweating and dyspnea or dizziness on exertion. Occasionally, the dyspnea may be extreme. There is usually an associated tachycardia. The blood pressure, particularly the systolic, tends to be elevated but variable. Sighing and yawning are common stigmas. This condition, which is probably of nervous rather than of cardiac origin, calls for sum-

mary rejection unless it is very mild. It should be noted that the syndrome is rather closely simulated in men who have, the night before examination, been on an alcoholic debauch.

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When all is said and done, it must be admitted that a man is no stronger than his cardiovascular system, and that this system may be subjected

TABLE 1. *Rejections Due to Cardiovascular Abnormalities in 1940 (8708 Men).*

CAUSE OF REJECTION	NO. REJECTED
Essential hypertension	39
Rheumatic heart disease	15
Mitral stenosis	4
Aortic regurgitation	2
Mitral regurgitation	1
Unspecified	8
Neurocirculatory asthenia	6
Organic heart disease, type unspecified	4
Tachycardia	4
Hypertensive heart disease	1
Auricular fibrillation	1
Total rejections for cardiovascular disease	70
Percentage of total examinations	0.8
Percentage of total rejections	4.9

to very severe strain over an indefinitely long period. We are increasingly convinced that the cardiovascular standards for admission to the United States Army should be of the strictest sort. Tables 1 and 2, which are derived from the work sheets of the Boston Induction Center, Fourth Recruiting Area, reflect this increasing conservatism and indicate in a general way the causes of rejection for cardiovascular defects.

It should be noted that the number and percentage of rejections for cardiovascular disease during the second period were materially greater than

TABLE 2. *Rejections Due to Cardiovascular Abnormalities in 1941 (8627 Men).*

CAUSE OF REJECTION	NO. REJECTED
Essential hypertension	88
Rheumatic heart disease	39
Mitral disease	14
Aortic disease	2
Mitral and aortic disease	1
Unspecified	22
Neurocirculatory asthenia	36
Organic heart disease, type unspecified	10
Tachycardia	8
Congenital heart disease	2
Auricular fibrillation	1
Paroxysmal tachycardia	1
Multiple extrasystoles	1
Total rejections for cardiovascular disease	186
Percentage of total examinations	2.1
Percentage of total rejections	13.3

those during the first. This difference is due to the increasing belief on the part of the examiners that the standards for acceptance (Class 1-A) must be of the strictest sort. This opinion has been concurred in by recognized cardiovascular experts.

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## NEW PHYSICAL STANDARDS FOR ARMY PILOTS

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BOSTON

CIVILIAN physicians are aiding the national wartime program greatly through their work in examining selective-service registrants both as voluntary examiners for local selective-service boards and as specialists at Army induction centers. As a result, many physicians are informed about the physical standards required for general military service. There is a different and higher standard, however, for military aviation. With this phase of physical examination for military service, private physicians have had little opportunity to become familiar. This paper describes briefly the requirements for qualification as an airplane pilot in the Army of the United States, as changed December 17, 1941, to meet wartime requirements.

Why should a private physician know something of this? In the first place, there is the medical man's catholic interest in affairs pertaining to his profession. Beyond that, the medical profession has already indicated its zeal in furnishing all possible assistance to the Nation during the present emergency. Such information as this article provides should fit a physician more fully for possible future service of even wider scope.

For those in private practice, there is also a service to be rendered to their patients in this connection. During the month of July, 1941, nearly 1300 New England men between the ages of twenty and twenty-six years, inclusive, applied for examination as Army aviation cadets. Before making official application, many of them went to their own physicians for advice about whether their physical condition warranted the effort and expense of securing an examination from the United States Army. Seldom was the physician in a position to offer advice based on a knowledge of the requirements.

No private doctor is authorized to qualify physically a candidate for the Army Air Corps. Official qualification must be determined by a special Army examining board, which includes a flight surgeon or medical officer and at least another officer. To become a flight surgeon, a medical officer must first take a special course in aviation medicine, during which he observes the effects of flight and high altitudes on physique, as well as on other phases of medicine peculiar to aviation. After successfully completing such

a course, he is authorized to term himself "A.M.E." (aviation medical examiner). If he fulfills his duties in a satisfactory manner as an aviation medical examiner for at least a year, the chief of Army Air Corps may certify him as a flight surgeon.

Even though the private physician cannot qualify a candidate officially, he may be in a position to save his patient from considerable effort and disappointment—that is, he can advise certain patients who may come to him for advice about the possibility of their entering the Air Corps that they definitely will not be able to meet the physical standards. In other cases, the private physician is in a position to encourage ambitious young men to go ahead with their applications as good risks to pass the physical examination. All this would be a service to the Army as well as to the applicant. It would relieve the pressure on the Air Corps examining boards by saving them the fruitless task of examining a large number of applicants who could have been advised earlier that they were not physically suitable.

Of the 1287 men examined during the month of July, 567 were definitely rejected; 589 qualified, and 131 others were tentatively rejected, pending correction of minor defects. Since it takes an average of four hours for the complete examination of one man, the pressure on the Air Corps examining boards is obvious.

Army aviation cadets receive commissions on graduation from the course in flying; their value as future officers must be therefore considered. A number of young men who can qualify physically are not acceptable as aviation cadets because they lack qualities considered vital for a competent officer. Many of these, however, may be eligible for training as sergeant pilots.

Applicants who have had at least two years of college training are exempt from educational examination. Among such college men, the percentage of disqualification has been much smaller than among applicants who lack such training. But young men who have not had college opportunities are also eligible for aviation-cadet training if they pass a written examination in such subjects as algebra, plane geometry, plane trigonometry and English composition. Throughout New England, under the general leadership of the New England Aviation Cadet Committee, these men are being helped to prepare for such examina-

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tions by "refresher courses" given at extremely small fees through state and local departments of education, and through such fraternal and patriotic organizations as the Elks, American Legion and Veterans of Foreign Wars. It is expected that the educational requirements will be revised in the near future to meet the wartime need for manpower.

Candidates for appointment as Army aviation cadets must be male citizens (for at least ten years) of the United States, who at the time of application have reached their twentieth, but who have not reached their twenty-seventh birthday. They may be married only if they sign a statement that their dependents have other means of support. They must be of excellent character and sound physique, and in excellent health. Those who qualify have a splendid opportunity, both in the military service and for later civilian careers in private aviation. As aviation cadets, they are given thirty-five weeks of pilot training, West Point style. During this training, they receive \$75 a month in addition to their food, clothing, lodging, medical and dental care, and a \$10,000 life-insurance policy. On completion of the training, they are appointed second lieutenants, Air Corps Reserve, and are assigned to active duty. While on active duty, they receive an initial lump sum of \$150 to cover expenses for officer's uniform, are paid \$245.50 a month, and receive a cash bonus of \$500 for each year they serve on active duty. Obviously, it is a most desirable appointment.

The following discussion of physical standards is based on Army Regulations 40-105, covering the physical standards and examination procedure for the Form-63 examination of candidates for commissions. These standards are modified for flying duty, particularly those of vision. Their strict observance is considered necessary for the protection of the individual concerned and of those with whom he is associated in Army Aviation.

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*History.* An intensive examination of the past history of the candidate and of his family is conducted to determine abnormalities that might reveal disqualifying facts. In particular, the patient is questioned to determine the presence of constitutional disease, psychopathic tendencies or previous severe injuries, and evaluation is made regarding possible present or future handicaps as a result of them.

*Eye examination.* This is a most intensive phase of the examination, and more candidates fail to meet the eye standards than any other. Better

vision is obviously necessary for an airplane pilot than for an officer in another branch of the service. The following conditions are disqualifying:

Visual acuity less than 20/20, as tested by the ordinary Snellen chart or self-illuminating test cabinet. The applicant must be able to read the "20 line" of the Snellen chart from 20 feet perfectly, and without difficulty. Candidates with superior acuity are able to read the smallest or "15 line" from 20 feet, and are given a rating of 20/15.

Trachoma, or xerophthalmia; chronic conjunctivitis; pterygium encroaching on the cornea; complete or extensive destruction of the eyelids, disfiguring cicatrices and adhesions of the lids to each other or to the eyeball; inversion or eversion of the eyelids, or lagophthalmos; trichiasis, ptosis, blepharospasm or chronic blepharitis; epiphoria, chronic dacryocystitis or lachrymal fistula; chronic keratitis, ulcers of the cornea, staphyloma or corneal opacities encroaching on the pupillary area and reducing the acuity of vision below the standard noted above; irregularities in the form of the iris, or anterior or posterior synechias sufficient to reduce the visual acuity below the standard; opacities of the lens or its capsule sufficient to reduce the acuity of vision below the standard, or progressive cataract of any degree; extensive coloboma of the choroid or iris, absence of pigment, glaucoma, iritis, or extensive or progressive choroiditis; retinitis, detachment of the retina, neuroretinitis, optic neuritis or atrophy of the optic nerve; loss or disorganization of either eye, or pronounced exophthalmos; pronounced nystagmus, or permanent or well-marked strabismus; diplopia or night blindness; abnormal conditions of the eyes due to diseases of the brain; malignant tumors of the lids or eyeballs; asthenopia accompanying any ocular defect.

Color blindness. Defects of color vision are frequently discovered in men unaware of their presence. Ishihara's or Stilling's test charts are used for the determination of color vision, in addition to the Holmgren wool yarns. Some persons can select the six cardinal colors correctly but have difficulty with the various shades or mixtures. Such men will show color defects when tested with a set of pseudoisochromatic plates (American Optical Company) or the Ishihara plates, and they are disqualified if they miss more than 25 per cent of the plates. A pilot must have normal color vision for many reasons, among others the frequent use of colored lights for night landings and signal operations. There

exists a widespread false belief that color-blind persons are accepted by the Air Corps as observers. This is a myth. The false belief has been traced to a journalist's speculation concerning whether a color-blind observer might not be effective in detecting camouflaged objects because the camouflage was designed for normal eyesight. It is an interesting speculation, but tests have not proved its truth. The value of color blind observers in the field of camouflage detection is questionable, and candidities showing color vision defects are not acceptable for pilot training.

*Ears, nose and throat* Hearing, which is tested by the whispered voice test and the audiometer, when available, must be 20/20 in each ear. On otoscopic examination, there must be no evidence of a serious past inflammatory process that has resulted in sequelae interfering with the auditory or vestibular functions. In the examination of the nose and throat, distinction is made between permanent and temporary disqualifying conditions. For example, marked chronic enlargement of the tonsils or a deviation of the nasal septum sufficient to produce mouth breathing is temporarily disqualifying. After the correction of such temporary defects, a candidate is acceptable, but any irremediable defect or abnormality that materially interferes with the respiratory or olfactory function or with phonation disqualifies permanently. Consideration will show how essential it is for a pilot to have ears, nose and throat in excellent condition, especially when he flies at high altitudes and is thus subject to conditions outside those met in earth bound pursuits.

*Dental examination* Applicants must have a minimum of twelve teeth, which must include three serviceable natural masticating teeth above and three below opposing, and three serviceable natural incisors above and three below opposing. A satisfactory fixed prosthetic appliance may be considered serviceable, provided there is no evidence of infection or degeneration resulting from the pressure caused by the appliance. On the other hand, a removable plate or bridgework is not acceptable as a replacement for natural teeth. Disqualifying dental defects include gross prognathism, gross malocclusion and chronic gum infections, such as marked pyorrhea alveolaris.

*General physical examination* This is similar to the examination prescribed for selective service trainees in Mobilization Regulations 1-9. Care is exercised to detect any abnormalities of the cardiovascular, respiratory, gastrointestinal, endocrine and genitourinary systems. Muscles, bones and joints are carefully examined to determine freedom of motion, muscular co-ordination and evidence of previous disease or injury. The existence

of any form of organic heart disease is disqualifying. A systolic murmur at the apex that is transmitted to the axilla or angle of the scapula disqualifies. A cardiac murmur must be carefully investigated, and electrocardiograms and 6 foot films of the heart taken in an effort to determine whether the murmur is organic or physiologic in origin. Disqualifying is a heart rate of 100 or over, or of 50 or under, when this is proved to be persistent in the recumbent position; or a persistent systolic blood pressure of 140 or over for applicants under twenty five years of age or of 150 or over for those twenty-five years of age or older.

*Height and weight.* To be eligible, a candidate must be between 64 and 78 inches in height. His weight must be between 115 and 217 pounds and must be in proportion to his height. Evidence of obesity, with retarded development of the secondary sex characteristics, or evidence of gynecomastia or cretinism is disqualifying. Cases of underweight are investigated to determine the possibility of constitutional disease, such as tuberculosis, diabetes mellitus or hyperthyroidism.

*Neuropsychiatric examination.* Reflexes, gait, co-ordination and tremors are observed for any disqualifying indications. The function of the cranial nerves is examined, and all abnormalities reported. In addition, the experienced flight surgeon estimates whether the applicant is temperamentally fitted for aviation and appears "adaptable to military aeronautics."

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It is hoped that the foregoing will give civilian physicians a better understanding of the requirements for Army aviation cadets. In addition to helping the physician advise a patient who may be considering entering the Army Air Corps, it may be a helpful guide when young men appear to request help in correcting minor defects so that they may become physically qualified. Common remediable defects include deviation of the nasal septum, hypertrophied tonsils, carious or insufficient teeth, gum infections, overweight and underweight, hernias and varicoceles.

The purpose of these regulations is to conserve life and matériel by selecting for flying duty only men who are physically and mentally fit for such duties. It is, of course, necessary to maintain this standard, and further examinations are therefore made from time to time, with the result that newly developed defects may cause reclassification into lower brackets, either temporarily or permanently.

Equipped with this information, the medical profession should be better able to help their own patients and to serve their country in promoting the slogan—"Keep 'Em Flying."

## ARTERIAL OCCLUSION IN RELATION TO EFFORT\*

## With Special Reference to the Retinal Arteries

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**A**MONG the problems of industrial employment of persons with cardiovascular disease, there is none more troublesome than the determination of the relation between vascular obstruction and the work being done at the time of the attack. In coronary occlusion, evidence has failed to prove that a given physical effort can be considered responsible for the closure of the artery, although some studies suggest that subintimal hemorrhage, with or without rupture into the lumen from an atheromatous ulcer, may be precipitated by exertion. This, however, is a matter of speculation, and complete or relative inactivity appears to be the state most commonly present at the time of acute cardiac infarction.<sup>1,2</sup> This observation appears statistically significant even when the usual proportionate time spent by people at rest and while exercising is evaluated.

Although cases of coronary closure during work come most frequently into court for adjudication, there are other types of arterial occlusion in which the relation to exertion becomes a matter of medicolegal interpretation, namely, peripheral embolism and thrombosis, and arterial blocking from spasm or endarteritis. Perhaps the most dramatic is that resulting in sudden loss of eyesight from obstruction to the retinal artery. A case of this sort was the stimulus to the present study.

A sixty-one-year-old man with rheumatic and arteriosclerotic heart disease and aortic stenosis was working as a janitor. He did not complain of cardiac symptoms, and the heart showed normal rhythm except for premature beats. He was tending the fires, and when he opened the furnace door, a slight explosion occurred with a puff of coal gas. He stepped back from the flash and noticed sudden loss of sight in the left eye. He continued to work and carried ash barrels in the afternoon. Following this, he noted tingling in his left arm and foot, and twelve hours later developed paralysis of this side. It was claimed that the effort and excitement of stepping back from the explosion resulted in occlusion of the retinal

artery by an embolus projected from the heart. A review of our experience, which was undertaken in an attempt to discover the probabilities in such a case, was extended to involve a study of other types of arterial occlusion in ambulatory patients in relation to the precise effort that they were undergoing at the time of the attack.

It can easily be seen by a study of hospital records that most emboli, pulmonary and peripheral, occur when the patients are at rest in bed, either postoperatively or suffering from cardiac failure. We are not concerned with this group, since we are interested in discovering what a person, in a presumably ordinary condition of health, may be doing when peripheral embolism or thrombosis occurs.

The patients are divided into two groups: those with and those without eye symptoms. We have 29 patients in the former, with thirty attacks of occlusion, and 46 in the latter, with forty-seven occlusions. Both groups present diagnostic difficulties, particularly patients with retinal-artery occlusion. It is not often necessary to remove such eyes surgically, and the pathologic condition cannot be confirmed by examination. Such occlusion may be due to embolism, thrombosis, endarteritis (at times, syphilitic), prolonged spasm of the artery, as in acute quinine poisoning, aneurysm of the carotid system, cardiac inhibition from painful stimuli, severe hemorrhage, as in bleeding peptic ulcer, or combinations of these factors. In many cases, no obvious general disease is present. It should be understood that we are confining the problem to arterial and not venous occlusion. The latter is about four times as common as arterial obstruction, according to Minton.<sup>3</sup> The retinal picture of arterial blocking is that of ischemia, often with the characteristic cherry-red spot at the macula, and not the gross hemorrhage that is seen in venous obstruction. It seems generally agreed, however, that although embolism of the central artery of the retina remains a popular diagnosis, such embolism is relatively rare, and that obliterating endarteritis with thrombosis is the common cause. According to Kern,<sup>4</sup> no source of embolus can be found in over 66 per cent of the cases. However, cases of bilateral occlusion are *extremely*

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rare. In any event, the cardiac conditions that are most commonly associated with intracardiac thrombi should present the best presumptive background for embolism—cardiac infarction, mitral stenosis, auricular fibrillation or subacute bacterial endocarditis. This last condition does not appear in our series, since such patients are very rarely able to work beyond the earliest stages of the disease.

Several studies of the condition have been made, and many individual case reports published, particularly with reference to therapy in those with embolism, such as the use of amyl nitrite, icetyl choline, heparin and massage of the eyeball. We have failed to find any extensive series analyzed with a consideration of the exact activity at the time of the vascular accident. Minton's remarks that such occlusion of the retinal vessels rarely occurs in young people (10 per cent), when it is usually the result of valvular disease of the heart, in over 90 per cent of the cases the lesion appears after fifty years of age, and is due to gradual obliteration of the arteries with final abrupt closure. In his series of 64 cases, activity of the patient at the time of the loss of eyesight is described in only 4: a twenty-three year old woman with mitral stenosis on getting out of bed ten days after a second delivery, a forty-seven year old man with a normal heart on the day following severe hematemesis, a sixty-nine year old man during an attack of influenza, and a forty-eight year old woman who was walking in the street. Minton states, however, that occlusion of the artery may occur at any time of the day, although in most cases it happens in the early hours of the morning. He believes that a slight fall in blood pressure results in a diminished flow to the retinal artery and collapse of a half occluded vessel, with thrombosis and permanent occlusion, but admits that spasm may be a factor.

De Schweinitz and Holloway, in 1908, described 5 cases: a fifty-two year old man with arterio-sclerosis and probable hypertension, who lost his eyesight after many hours of proofreading, a thirty-two year old Negress with an enlarged heart and questionable syphilis, who awoke in the morning with blindness of the left eye, a thirty-two year old woman with mitral stenosis, who lost her vision while giving a massage treatment, a forty-five year old man, who became blind while riding index cards, and a nineteen year old boy with a normal heart, who lost his eyesight while dressing.

Coverdale,<sup>9</sup> in 1929, found 51 cases in the literature and added 11 of his own: a twenty-four year old girl with mitral stenosis, while washing her

hands, became blind in the right eye, a thirty-eight year old woman with mitral stenosis, while riding in a bus, lost the sight of the left eye, a twenty-one year old woman with mitral stenosis and aortic regurgitation awoke with loss of sight in the right eye, a sixteen year old girl with mitral stenosis awoke with blindness of the left eye, a nineteen year old boy with mitral stenosis, while sitting up in the morning, became blind in the right eye, a twenty-one year old woman with a suspicious first heart sound, while making beds, lost the vision of her left eye, a sixteen year old girl with a normal heart became blind in the evening, after swimming in the afternoon, a thirty-six year old man with mitral stenosis and aortic regurgitation, while reading after work, lost the sight of his right eye, a seventy year old man with an enlarged heart, an aortic systolic murmur and a complete heart block, while dressing, slipped but did not fall, and suddenly lost sight in the left eye, a fifty-two year old man with a normal heart, while walking, became blind in the right eye, a sixty-five year old man with an enlarged heart and aortic systolic murmur, while sitting down, noticed that the vision became dim in the left eye—it was better the next day, but he was almost blind the following day.

In these 20 cases from the literature, no loss of vision occurred when the patient was undergoing severe or unusual exertion, 14 cases occurred with mild or moderate effort, and 6 when the patients were at rest.

In 3 of de Schweinitz and Holloway's cases, preliminary symptoms of transient blindness or hazy vision occurred at times prior to the permanent blindness. This suggests in element of spasm or, possibly, transient ischemia from reduced blood flow and, less likely, small emboli before the complete occlusion. Both spasm and emboli small enough to pass into less important retinal vessels have been observed on ophthalmoscopic examination of the retina. Some authors have thought that spasm was precipitated by effort, and that physical exertion should be reduced in patients with a history of transient blindness. In permanent loss of vision from occlusion of retinal vessels, effort appears to play no part. The situation has been compared to angina pectoris, in which unusual effort may precipitate an attack but cardiac infarct from closure of a coronary vessel, or final cumulative ischemia, does not appear to be related to physical exertion. Similarly, it is not unusual for a patient with intermittent claudication from arteriosclerosis of leg vessels to have pain on effort, but to have the final episode, which results in gangrene, appear at rest. In such cases, con-

plete arterial occlusion may not be demonstrable in the amputated specimen.

It might be argued that an increase in the activity of the heart, resulting in increased output and blood velocity, might lead to the dislodgment of mural thrombi and thus result in embolism, and,

Fifteen cases of rheumatic heart disease were studied. The ages ranged from twenty to forty-nine years. There were 12 men and 3 women. One man had two occlusions. Nine patients had auricular fibrillation, 5 had normal rhythm, and 1 had questionable auricular fibrillation. Loss of

TABLE 1. *Occlusion of Retinal Artery.*

CASE No.	AGE	SEX	CLINICAL DIAGNOSIS	CAROTID RHYTHM	EYE AFFECTED	ONSET OF BLINDNESS
1	26	M	Rheumatic heart disease, aortic regurgitation and stenosis	Auricular fibrillation	Right	On awaking in morning
2*	26	M	Rheumatic heart disease, aortic regurgitation and stenosis	Normal	Right	While working in hospital dispensary
3	40	M	Rheumatic heart disease, aortic regurgitation and stenosis	Normal	Right	On blowing nose while walking
4	34	M	Rheumatic heart disease, mitral regurgitation and stenosis	Auricular fibrillation	?	While resting after long ride in automobile
5	38	M	Rheumatic heart disease	Auricular fibrillation	Left	While reading aloud
6	35	F	Rheumatic heart disease	Auricular fibrillation	Right	On awaking in morning
7	28	M	Rheumatic heart disease	Auricular fibrillation	Right	While stooping forward
8	29	M	Rheumatic heart disease	Auricular fibrillation	Right	While bending forward
9	20	M	Rheumatic heart disease	Normal	Right	While sitting at movies
10	22	M	Rheumatic heart disease	Normal	Right	While playing baseball
11	48	M	Rheumatic heart disease	Normal	Left	While lifting or pulling
12	48	M	Rheumatic heart disease	Auricular fibrillation	Right	On awaking in morning
13	46	F	Rheumatic heart disease	Auricular fibrillation	Left	While reading
14	38	M	Rheumatic heart disease	Auricular fibrillation	Right	While reading
15	49	M	Rheumatic heart disease	Auricular fibrillation	Right	On awaking in morning
16	55	F	Hypertension	Auricular fibrillation	Right	While dressing in morning
17	60	F	Hypertension	Normal	Left	While sweeping
18	56	F	Hypertension	Normal	Right	While doing housework
19	66	M	Hypertension	Normal	Left	While sitting at movies
20	61	M	Hypertension	Normal	Right	On bending forward while at work on automobile
21	81	F	Hypertension	Normal	Right	On awaking in morning
22	63	M	Hypertension	Normal	Right	While turning head quickly
23	61	M	Arteriosclerosis and probable rheumatic aortic stenosis	Premature beats	Left	While stepping back from furnace explosion
24	75	F	Arteriosclerosis	Normal	Left	While dressing in morning
25	44	M	Syphilis	Normal	Right	While walking about house
26	51	F	Syphilis and hypertension	Normal	Left	While ironing
27	28	M	None	Normal	Left	While walking
28	23	F	None	Normal	Right	While sleeping
29	35	M	None	Normal	Left	While listening to radio

\*While lying in bed receiving digitalis, this patient had an attack of blindness in the other eye—six days after an attack of paroxysmal auricular fibrillation.

conversely, that a slowing of the blood stream might more logically be expected to promote thrombosis in the arterial system. The findings in our cases do not support the first part of this hypothesis, if the onset of symptoms can be considered coincident with the vascular blocking.

#### REVIEW OF CASES

##### *Occlusion of Retinal Artery*

The series of cases with occlusion of the retinal artery or its branches included 29 patients, with thirty attacks (Table 1).

sight came suddenly in the right eye in 10 cases, and in the left in 4. In 1 case with aortic stenosis and regurgitation and normal rhythm (Case 2), the right retinal artery was occluded first, and then the left.

It can be said that only 2 of these patients with a total of sixteen occlusions were undergoing unusual physical effort when overtaken by blindness. Six were engaged in mild exercise. Eight occlusions occurred when the patients were at complete rest. It is of interest that the man who had sudden loss of vision in his right eye on blowing his nose while walking (Case 3) was thought

possibly to have had mild typhoid fever some time before but was able to work sacking grain nine and a half hours a day without symptoms.

There were 9 cases of hypertension and arteriosclerosis, 1 of which was complicated by aortic stenosis; only 1 patient had auricular fibrillation. The ages ranged from fifty-five to eighty-one years. Five patients were women. The right eye was involved five times, and the left eye four times. Two patients were doing housework, including sweeping, 1 stepped back from a slight furnace explosion, 1 was bending forward working on an automobile, 2 were dressing, 1 awoke with loss of vision, 1 was at the movies, and 1 noticed loss of vision with a quick turn of his head. Perhaps the man at work on the automobile (Case 20) was engaged in unusual effort. The case of the janitor (Case 23) is questionable. None of the others could reasonably blame their occupations. Endarteritis with thrombotic occlusion seems the best explanation for these cases, with the possible exception of the patient with auricular fibrillation (Case 16), in whom embolism may have occurred.

Two patients were syphilitic: one, a fifty-one-year-old woman (Case 26), also had hypertension; the other (Case 25) was a man of forty-four. Both patients had normal cardiac rhythm. The woman lost the sight of her left eye while ironing, two days after premonitory symptoms lasting ten minutes. The man walked home on a cold day, drank a small glass of whisky and, while walking about the house an hour later, became blind in the right eye. No relation to effort seems apparent in these cases, and endarteritis is the probable cause. Spasm may have been a factor in Case 26.

Three patients in whom no heart or general vascular disease was found were as follows: a twenty-eight-year-old woman who went blind in the left eye while she was walking, a thirty-five-year-old man who lost vision in the left eye while sitting listening to the radio, and a thirty-three-year-old woman who became blind in the right eye while she was asleep. Blood serologic findings were negative for syphilis in all 3 cases. Two patients in this group were at rest, and 1 was engaging in mild effort.

These 30 cases of occlusion of the central artery of the retina, or its branches, occurred in 29 patients. Three patients were engaged in rather strenuous physical effort and, 15 in mild to moderate effort, and 12 were at rest.

#### *Nonretinal Arterial Occlusion*

In a series of 46 cases, with forty-seven attacks, the occlusion was not in the vessels of the eye (Table 2).

Twenty-two patients with rheumatic heart disease—14 women and 8 men—were included. The ages ranged from twenty-six to sixty years. Four patients had normal rhythm, and 18 had auricular fibrillation; 3 had multiple occlusions. Of the whole series, 9 patients had occlusions of the cerebral vessel, 12 had occlusions in the arteries supplying the legs, and 5 had occlusions in the arms. In this group, it is likely that the occlusions were due to emboli from auricular thrombi arising from the combination of mitral stenosis and auricular fibrillation.

In no case did the embolism occur during violent effort. In 2 cases, it happened some time after unusual effort: in one (Case 43), fifteen minutes after running for a trolley, and in the other (Case 47), after the patient had fixed a bed. In 9 cases, embolism occurred during mild effort, such as rising in the morning, driving a car and eating breakfast. In this group, 2 patients (Cases 37 and 44) were somewhat more strenuous, one playing golf, and the other working as a baker. In 11 patients, or half this group, embolism occurred while the patients were at complete rest.

Twenty-three patients with arteriosclerosis or hypertension, or both,—15 women and 8 men,—who had sudden vascular occlusions were studied. The ages ranged from forty-five to eighty-two years. One other patient, a man of forty, without demonstrable cardiovascular disease (Case 75), was also observed. He had a sudden embolus to the left posterior tibial artery, with recovery following embolectomy. The sites of the occlusion in twenty-five occlusions in 24 patients were as follows: brain, 3; legs, 19; arms, 2; and abdomen (superior mesenteric artery), 1. Auricular fibrillation was present in 10 patients (possible paroxysmal auricular fibrillation in 2), premature beats in 2, complete heart block in 1, and normal rhythm in 11. In no case was the patient engaged in severe or unusual effort, and 12 patients were at complete rest.

#### DISCUSSION

It is essential to determine the relation between arterial occlusion caused by embolism, thrombosis, endarteritis or vascular spasm, and the physical effort engaged in by the patient at the time of the episode or for an indefinite interval preceding it. This relation may determine not only the responsibility of the effort for the occlusion, but also the wisdom of insisting on inactivity for victims of cardiovascular disease.

In the series here presented, embolism appears to be the likeliest mechanism for occlusion in the 38 cases in which auricular fibrillation was pres-

TABLE 2 *Peripheral Arterial Occlusion Exclusive of Retinal Vessels.*

CASE No.	AGE	SEX	CLINICAL DIAGNOSIS	CARDIAC RHYTHM	POSITION OF OCCLUSION	ONSET OF OCCLUSION
30	35	F	Rheumatic heart disease mitral stenosis	Normal	Cerebral artery	While lying in bed three days post partum
31	56	F	Rheumatic heart disease, aortic regurgitation and stenosis mitral regurgitation and stenosis and hypertension	Auricular fibrillation	Cerebral artery	While getting out of bed
32	51	F	Rheumatic heart disease mitral stenosis	Auricular fibrillation	Cerebral artery	While sitting after supper
33	45	F	Rheumatic heart disease mitral stenosis	Auricular fibrillation	Cerebral artery	While lying in bed
34	39	F	Rheumatic heart disease mitral stenosis and regurgitation and aortic regurgitation	Auricular fibrillation	Cerebral artery	While eating breakfast
35	41	F	Rheumatic heart disease mitral stenosis	Auricular fibrillation	Left leg	While lying in bed
36	59	F	Rheumatic heart disease mitral stenosis	Auricular fibrillation	Left leg	While driving automobile
37	48	M	Rheumatic heart disease	Auricular fibrillation	Left leg	While playing golf
38	48	F	Rheumatic heart disease mitral stenosis	Auricular fibrillation	Femoral artery	While lying in bed
39	54	M	Rheumatic heart disease mitral stenosis	Auricular fibrillation	Right and left femoral and left brachial arteries	While working as clerk
40	49	F	Rheumatic heart disease	Auricular fibrillation	Iliacal artery	While sitting in chair
41	49	F	Rheumatic heart disease	Normal	Legs, arms and brain	On awaking
42	26	F	Rheumatic heart disease	Auricular fibrillation	Cerebral artery	While sitting in chair
43	33	M	Rheumatic heart disease mitral stenosis aortic regurgitation	Auricular fibrillation	Leg	Fifteen minutes after running for trolley
44	32	M	Rheumatic heart disease mitral regurgitation and stenosis	Normal	Left brachial artery	While working as baker
45	60	M	Rheumatic heart disease mitral regurgitation and stenosis	Auricular fibrillation	Left posterior tibial artery	After heavy day's work
46	39	F	Rheumatic heart disease mitral regurgitation and stenosis	Auricular fibrillation	Left leg	On returning to bed at midnight
47	38	M	Rheumatic heart disease mitral stenosis	Auricular fibrillation	Left arm and (15 minutes later) both femoral arteries	After fixing a bed
48	45	F	Rheumatic heart disease mitral stenosis	Auricular fibrillation	Left iliac artery	In evening while quiet
49	55	F	Rheumatic heart disease mitral stenosis	Auricular fibrillation	Right leg	While getting out of bed in morning
50	52	M	Rheumatic heart disease mitral stenosis	Auricular fibrillation	Cerebral artery	While getting out of automobile
51	52	M	Rheumatic heart disease slight aortic regurgitation mitral regurgitation slight hypertension	Normal	Cerebral artery	On awaking in morning
52	55	F	Hypertension mitral stenosis, ? rheumatic heart disease	Auricular fibrillation	Cerebral artery	While cooking
53	56	F	Arteriosclerosis	Auricular fibrillation	Cerebral artery	While sitting talking
54	55	F	Hypertension	? Paroxysmal auricular fibrillation	Cerebral artery	While walking up hill
55	56	F	Hypertension	Auricular fibrillation	Superior mesenteric artery	While cleaning house
56	70	M	Arteriosclerosis	Normal	Left leg	While lying in bed
57	82	F	Arteriosclerosis	Auricular fibrillation	Left leg	On awaking
58	67	F	Arteriosclerosis	Normal	Left leg	While reading
59	74	M	Arteriosclerosis	Normal	Right femoral artery	Following emesis
60	51	M	Arteriosclerosis and hypertension	Auricular fibrillation	Right femoral artery	While walking
61	71	F	Arteriosclerosis and hypertension	Normal	Left femoral artery	While in bed
62	58	M	Arteriosclerosis and hypertension	Normal	Iliac artery	While working as conductor
63	64	F	Arteriosclerosis and diabetes	Auricular fibrillation	Bifurcation of iliac arteries	On awaking at 1:30 in morning
64*	45	F	Arteriosclerosis	Auricular fibrillation	Leg	While doing housework
65	59	M	Arteriosclerosis	Auricular fibrillation	Leg	While at home with cold



TABLE 2 (Concluded).

C. No.	Age	Sex	CLINICAL DIAGNOSIS	CARDIAC RHYTHM	POSITION OF OCCLUSION	ONset OF OCCLUSION
66	50	F	Arteriosclerosis	Normal	Left leg	While sitting on doorstep
67	63	M	Arteriosclerosis and hypertension	Normal	Left leg	While sitting at supper table
68	64	F	Arteriosclerosis and diabetes	Auricular fibrillation	Both popliteal arteries	On getting out of bed in morning
69	80	F	Arteriosclerosis and hypertension	Complete heart block	Right leg	While getting out of bath tub
70	60	F	Arteriosclerosis and hypertension	Paroxysmal auricular fibrillation or premature beats	Left brachial artery	After doing housework
71	49	F	Arteriosclerosis and hypertension	Auricular fibrillation	Right common iliac artery	While sitting on edge of bed
72	67	M	Arteriosclerosis, late syphilis, acute alcoholism	Normal	Right popliteal artery	On awaking
73	74	F	Arteriosclerosis and hypertension	Normal with premature beats	Left arm	While sitting after working in kitchen
74	69	M	? Arteriosclerosis	Normal	Leg	While sitting in chair
75	40	M	No heart disease proved	Normal	Left posterior tibial artery	While walking

\*While lying in bed, this patient later had another occlusion in the leg.  
 †Patient later had an occlusion of the left arm.

ent, as well as in the 37 cases of rheumatic heart disease with or without auricular fibrillation—in 10 nonretinal cases, operation or autopsy proved this to be so. Local vascular disease, with or without spasm, was the probable cause in the other cases.

Some observers have recently suggested the transfer of the blame for sudden coronary occlusion into a rather remote past, claiming that events and activities in the life of the patient, days or even weeks prior to the occlusion, could be held responsible. Such a view opens the way to tremendous legal complications. Certainly, arterial embolism cannot be included in such a hypothesis, and this study concerns only the immediate precipitating factor. The question is, Does the effort in which the patient is engaging just prior to, or during, the occurrence of embolism have anything to do with washing off intracardiac material and releasing it into the blood stream? On a priori grounds, it seems that strenuous effort might do just this.

However, in our 38 patients with auricular fibrillation, in whom speeding of the blood stream by effort might conceivably be such an excitant of embolism, the occlusion occurred only twice a few minutes after severe effort, sixteen times with mild to moderate effort, and twenty times at rest. It may be objected that cardiac patients with auricular fibrillation, or older arteriosclerotic persons, cannot engage in violent effort to prove or disprove this assumption. Our figures suggest,

however, that there is no reason to suspect that the ordinary activities of the patients' lives are likely to precipitate embolism; that unusual effort is not an expected cause of arterial occlusion; and that the mechanisms of arterial blockage are as progressive when the patient is at rest as when he is active, and perhaps more so.

In this group of seventy-seven occlusions, sudden loss of eyesight, or of the use of a limb, or occlusion of cerebral or mesenteric vessels, based on embolism or other arterial blockage, occurred during ordinary daytime activities, or when the patients were at rest, in over 9 out of 10 cases.

#### SUMMARY AND CONCLUSIONS

Seventy seven attacks of acute arterial occlusion in 75 ambulatory patients are described. 30 of these occurred in the retinal arteries of 29 patients, and 47 occurred in other peripheral arteries of 46 patients.

In 3 cases, the occlusion took place during rather severe effort, and in 2, a few minutes after unusual exertion; in 37, the occlusion occurred coincident with mild or very moderate effort, and in 35, when the patient was at rest in bed or sitting in a chair.

Peripheral arterial occlusion from embolism, thrombosis or endarteritis rarely occurs during unusual physical effort even in patients with cardiovascular disease of a degree compatible with quite strenuous exertion. In our series, such occlusion occurred approximately fourteen times as

commonly when the patient was at complete rest or when engaged in the ordinary exertions of his usual life.

In approximately half the entire series of arterial occlusion,—embolic and obliterative,—the patient was physically inactive. This suggests that the conditions necessary for either embolism or thrombosis are as effective with reduced as with increased blood flow, and that the occurrence of such an accident is at least fortuitous.

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## TUBERCULIN TESTS IN CHILDREN

### An Interpretation of a Series of Varying Intradermal Test Doses and of a Comparable Series of Patch Tests

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IT has been the usual custom to perform the intradermal or Mantoux tuberculin test in the Out-Patient Department of the Children's Hospital by injecting 0.1 cc. of old tuberculin diluted 1:1000. As a result of this dilution, an actual dose of 0.1 mg. of tuberculin comes in contact with the intracutaneous tissues. Although a weaker initial dose is occasionally used for patients suspected of strong tuberculin allergy, experience in this clinic has not led to apprehension that more than 0.1 mg. is too great an amount for routine testing. On the other hand, some doubts have arisen that it may not be strong enough to give dependable diagnostic evidence. Since patients are frequently brought to the clinic from a considerable distance and since their transportation usually involves at least one other person, it is highly desirable that repeated visits for retesting be avoided unless there is reason to believe that a negative response to the 0.1-mg. dose is unreliable.

Although most authorities advise that patients negative to 0.1 mg. be retested with 1.0 mg. (0.1 cc. of 1:100 dilution) of tuberculin, the percentage who react only to the larger dose is variably stated. Thus, Hart,<sup>1</sup> in the London investigation of 1929, found that 96.3 per cent of patients with known tuberculosis reacted to 0.1 mg., and that this percentage was raised to 97.3 by retesting the negative patients with 1.0 mg. In a series of controls from the general population, he found that 40.5 per cent reacted with 0.1 mg., whereas the percentage increased to 43.5 with the stronger dose. Lincoln,

Raia and Gilbert<sup>2</sup> have recently presented evidence to show that in New York City a much larger percentage of children negative to 0.1 mg. may react to increased doses. These authors found that 17 (10.9 per cent) of 155 such children reacted to 1.0 mg. The most striking data have come from the Lymanhurst studies. Harrington, Myers and Levine<sup>3</sup> published in 1937 their statistics on the sensitivity to tuberculin of over 4500 children and adolescents from five to eighteen years of age. Of this number, 8.7 per cent were positive to 0.1 mg. of tuberculin, but another 9.2 per cent of the total group were positive to 1.0 mg., although they failed to react to 0.1 mg. Thus, not even half the tuberculin-sensitive patients would have been discovered had the testing not been carried beyond the usual 0.1-mg. injection. In another context, Myers<sup>4</sup> cautions that "the administration of a sufficient dosage of tuberculin is important as a 10 to 20 per cent error may result from using only the small dose." Unfortunately, various series of data are not presented in a manner facilitating direct comparisons, but the experience with adults at the Boston City Hospital may be mentioned. Of 100 patients reacting to 1.0 mg. of tuberculin, 81 were found to react to 0.1, 48 to 0.01, and 14 to 0.001 mg. This indicates that an error of about 20 per cent would result from depending on 0.1 mg. as the test dose.

Such statements as these raise doubt concerning the validity of a clinic procedure in which all children negative to a routine strength of tuberculin are not called back for a stronger test. Therefore, a primary reason for the present study was to determine the error, if any, that might be avoided by performing these second tests on every infant and child not reacting to 0.1 mg.

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A second problem for consideration was the degree of reaction to which positive significance could be ascribed. This became significant particularly because of frequent errors in interpretation of tests read for us by visiting nurses and, in some cases, by health officers and family physicians. The error was almost always that of interpreting the faint redness of a dubious or negative test as positive, a mistaken impression later rectified by retesting with stronger solutions but only after considerable parental confusion, if not distress, had been brought about. In an attempt to avoid such difficulties and still to spare crowding of the clinic and unnecessary transportation of children, we now ask parents of patients living at a distance to measure the diameters of redness and of swelling at the injection site and to send us these objective data on a mimeographed postal card. Proper interpretation of such objective data requires as definite standards as possible. It should be mentioned in passing that indefinite reactions are not limited to outpatients but occasionally confuse the diagnostic data of ward patients as well, and that reference to the directions for interpreting tuberculin reactions as given in *Diagnostic Standards*\* does not always evaluate the dubious induration or the inconstant edema.

#### EXPERIMENTAL PROCEDURE

A quantitative testing procedure was devised to answer the two questions, What strength of tuberculin is sufficient to elicit a positive reaction? and What local manifestations constitute such a reaction? When a child in the hospital was discovered to react to the routine test with 0.1 mg. of tuberculin, and was not deemed an unfavorable subject because of fever, serious illness or other cause, he was retested on the other arm with simultaneous injections of 0.1, 0.01 and 0.001 mg. of tuberculin, respectively, or 0.1 cc. of 1:1000, 1:10,000, and 1:100,000 dilutions. The preparation used has been standard for many years in this hospital, and consists of O.T. (old tuberculin) supplied by the Saranac Laboratories and made up to the proper strength with carbolyzed saline solution. Fresh dilutions are made once a month and kept in refrigerators when not in use. In some patients whose original reactions to 0.1 mg. were very slight, the graded tests consisted of 1.0, 0.1 and 0.01 mg. In all cases, the sites of injection were spaced sufficiently far apart so that resultant erythemas would not coalesce, and the strongest solution was injected proximally so that lymphatic drainage could not carry more tuberculin into sites where smaller

amounts had been injected. These simultaneous graded tests were read at twenty-four, forty-eight, seventy-two and ninety-six hours thereafter, by outlining the extent of erythema and of induration on tracing paper placed over the reactions. So relatively scarce have tuberculin-positive children become in our wards that it was necessary to turn to another source to augment our series of such patients. At the North Reading State Sanatorium, through the courtesy and interest of Drs. Earle Willoughby and Gerald Caron, we were enabled to test 75 children in various stages of tuberculous disease and healing. In that institution, testing is not ordinarily made with doses stronger than 0.01 mg., and there seemed little reason for changing the procedure during this series of investigations, since children positive to 0.01 mg. would, of course, have reacted to 0.1-mg. tests also, and should give questionable reactions at the sites of still weaker doses. Accordingly, most of the North Reading children were tested only with 0.01 and 0.001 mg. of tuberculin. Some received 0.0001 mg. as well, but in every case simultaneous doses of at least two strengths were applied.

The combined groups from the Children's Hospital and the North Reading State Sanatorium furnished a total of 118 tuberculin-positive children who were tested in this general manner. In addition to these, another unselected group of about twice their number who did not react to tuberculin in the standard 0.1-mg. dose in our wards were tested with graded doses in the same way. In these, the tests usually consisted of doses of 0.1, 1.0 and 10.0 mg. Thus, 336 tuberculin-positive and tuberculin-negative children were injected with at least two and usually three simultaneous test doses (Table 1). From the results, it was possible to determine the number failing to react to 0.1 mg. but positive to 1.0 or to 10.0 mg. It was also hoped—and to some extent this hope was realized—that the responses would give some clue of what might be called a positive reaction, since weak or questionable reactions should be noted in children whose definitely positive responses to stronger amounts gave proof of their tuberculin sensitivity, just as there would also be doubtful responses in others proved by stronger tests to be tuberculin negative. Thus, a study of both types of borderline reactions might lead to criteria concerning the time of appearance and fading, degree of induration and so forth, which would guide our future interpretation of isolated questionable reactions.

This study also gave an excellent opportunity to compare the sensitivity of the Vollmer tuberculin patch test with the response of children to

\*In *Diagnostic Standards*, published in 1940 by the National Tuberculosis Association, edema is considered an essential of a positive reaction; edema of more than 5 and less than 10 mm. diameter is required for a + reaction.

various strengths of O.T. administered by the Mantoux technic. Accordingly, at the time graded tests were applied to one arm, the patch test\* was applied on the other arm, or more commonly on the upper back. The patches were removed after forty-eight hours, and read then and at seventy-two and ninety-six hours by the same tracing-paper technic. Thus, the study was made to answer a third question, What is the relative sensitivity of the Vollmer test as compared with the Mantoux test in various dilutions?

RESULTS

Adequate Tuberculin Dosage

The positive reactors from Table 1 have been listed in Table 2 with the percentage of children

If 70, instead of 7, per cent of our patients reacted to tuberculin, the group requiring more than 0.1 mg. would be larger but only proportionately so, and the percentage should therefore not change. An unquestionable testimony to the comparative accuracy of the 0.1-mg. dose appears when the results are contrasted with those using 0.01 mg. It will be noted from Table 2 that 84 per cent of those reacting to 0.1 reacted to 0.01 mg., whereas only about 40 per cent of the latter group were positive to 0.001 mg. Such great discrepancies appear between graded tests weaker than 0.1 mg., and so little increase in accuracy results from tests stronger than 0.1 mg. that we shall continue to consider it a satisfactory single-strength test for routine clinic purposes. It should be mentioned,

TABLE 1. Reactions to Simultaneous Tests in 119 Tuberculin-Positive and 217 Tuberculin-Negative Children Grouped according to Presumable Susceptibility.

GROUP	PRESUMABLE SUSCEPTIBILITY OF GROUP	No. OF CASES	REACTION •	AMOUNT OF O. T. IN TEST DOSE				
				10.0 MG.	1.0 MG.	0.1 MG.	0.01 MG.	0.001 MG.
A	None	208	Positive Negative	4 204	3 205	0 208		
B	Slight	13	Positive Negative		7 6	6 7	2 11	
C	Moderate	53	Positive Negative			50 3	36 17	20 33
D	Marked	62	Positive Negative				58 4	18 44
Totals		336		4+ 204-	10+ 211-	56+ 218-	96+ 32-	38+ 77-

reacting to any one dose expressed in terms of their response to a dose ten times as strong. Of 118 children who reacted to 1.0 mg., 97 per cent were found to react to 0.1 mg. Thus, in the Boston vicinity and in children younger than twelve years, the 0.1-mg. dose of tuberculin should bring to light all but 3 per cent of the positive reactors. Obviously, this will not apply everywhere, and it can be stated here only with qualifications. One reason for the practical accuracy of the test is the small number of tuberculin-sensitive persons in the clinic community, since the smaller that number is, the less frequently will one encounter the occasional state of mild allergy. A comparison of the amount of tuberculosis observed among our patients with that observed at older age levels and in different places cannot be included here. It may be stated, however, that in the last statistics available from children tested in the Out-Patient Clinic (with 0.1 mg. O.T.) the findings were: 0.7 per cent positive reactions among 190 infants under three years; 1.8 per cent among 315 children from three to five years; 2.7 per cent among 325 children from six to eight years; and 7.0 per cent among 220 children from nine to eleven years.

\*The test material was kindly furnished by the Lederle Laboratories, Incorporated, Pearl River, New York.

however, that in individual diagnostic problems in which the degree of allergy may be masked by

TABLE 2. Accuracy of Different Test Doses, as Shown by the Positive Reactors in Table 1.

GROUP	POSITIVE REACTORS	
	1.0 MG.	0.1 MG.
A	3	0
B	7	6
C	50*	50
D	58*	58*
Totals	118	114
Accuracy of 0.1 compared with 1.0 mg.		97%
	0.1 MG.	0.01 MG.
B	6	2
C	50	36
D	58*	58
Totals	114	96
Accuracy of 0.01 compared with 0.1 mg.		84%
	0.01 MG.	0.001 MG.
C	36	20
D	58	18
Totals	94	38
Accuracy of 0.001 compared with 0.01 mg.		40%

\*Not tested with this dose but reacted to weaker dose.

fever, intercurrent infections or very early or very far-advanced tuberculosis, adaptation of the dose to the patient may be necessary. The increasing

use of P.P.D. (purified protein derivative) necessitates some expression of the results mentioned above in terms of that preparation, but only a rough comparison is possible on the basis that 0.01 mg. of O.T. is about equivalent to the first-strength dose of P.P.D., and that 1.0 mg. O.T. may not elicit quite so many positive reactions as the second-strength dose.<sup>3</sup> We have not adopted P.P.D. as a routine tuberculin because of its expense and because the first-strength dose is too weak and the second-strength too strong for a routine single test; nevertheless, in occasional diagnostic difficulties requiring extreme accuracy of testing, the second-strength dose is a valuable check on strong doses of O.T.

#### True and False Positive Reactions

The 336 patients in this study were tested with a total of nearly a thousand individual Mantoux tests (Table 1). Of this total, the interpretations of a certain number were, as was anticipated, questionable, and thus would have been, as isolated tests, dubious in significance. Their characteristics are given below. Since the results from simultaneous stronger and weaker tests were available, it was hoped that some observations might be made by which these doubtful responses could be interpreted.

There were two main groups of questionable reactions: those in children whose simultaneous stronger tests proved them to be definite reactors; and those in children whose other tests, histories and physical findings gave no evidence to suggest tuberculin sensitivity. The first group might be called "weak positive reactions," and the second "false positive reactions" or "pseudo-reactions."

*Weak positive tests* showed an erythema 1 cm. or less in diameter, with extremely indefinite induration. Such responses, although they may fall in the + group according to *Diagnostic Standards*, and thus were listed as positives in Table 1, have occasionally been misleading and are always interpreted with hesitancy. An analysis of their characteristics as shown in this study is given in Table 3. It will be noted that an almost equal number of these weak responses was called forth by 0.001 and by 0.01 mg. of tuberculin, but their behavior was somewhat different when classified according to the dosage. Weak responses to 0.001 mg. showed a tendency to increase in area or to remain of the same size between the twenty-four hour and forty-eight-hour readings. Fading during this period was less common, so that two thirds still showed an area of erythema at least 2 mm. in diameter even after seventy-two hours. On

the other hand, similar weak responses to 0.01 mg. showed less tendency to increase in area or to hold their size with the passage of time, and a smaller number persisted to three days. It appears that the weaker the test dose used, the more

TABLE 3. *Number and Behavior of Weak Reactions in Children Definitely Positive to Stronger Doses.*

DOSAGE AND TYPE OF REACTION	No. OF TESTS
Weak reactions to 0.001 mg. O. T.	33
Increased or remained of same intensity from twenty four to forty eight hours	22
Faded in intensity from twenty four to forty eight hours	11
Some reaction still perceptible at seventy two hours	22
Weak reactions to 0.01 mg. O. T.	31
Increased or remained of same intensity from twenty four to forty eight hours	14
Faded in intensity from twenty four to forty eight hours	17
Some reaction still perceptible at seventy two hours	17
Weak reactions to 0.1 mg. O. T.	2

significant is a faint type of reaction, particularly if it does not diminish in intensity after the first twenty-four hours. In fact, this series of tests shows that any response of from 5 to 10 mm. in diameter at forty-eight hours might be interpreted as positive, provided it was called forth by a dose of 0.01 mg. or, better still, by one of 0.001 mg.

It is striking that with tests of 0.1 mg., although nearly three hundred were applied and a fifth were positive, only two weak reactions occurred. In one of these children, although a definite response was obtained with 1.0 mg., the 0.1-mg. test produced only 7 mm. of erythema (no induration) at forty-eight hours and complete fading by seventy-two. In the other, the 0.1-mg. reaction reached a height of 6 mm. of erythema and 2 mm. of induration at forty-eight hours, with an impalpable 3-mm. stain at seventy-two hours.

It is difficult to speak with complete certainty of *false positive reactions* or *pseudoreactions*, since by definition they must occur in tuberculin-negative children, and the presence of any sort of response to tuberculin makes one hesitate to call a person negative. However, these reactions differed sufficiently from the weak positives just described to make us believe that they had no positive significance. It will be seen in Table 4 that they were encountered most frequently with the stronger doses, only one occurring at the site of 0.1-mg. injections and none with any weaker dose. These reactions were characterized by rapid fading; thirty subsided entirely within forty-eight hours, although many were erythematous areas 3 cm. or even more in diameter at twenty-four hours, and a few were somewhat swollen though not defi-

nately indurated. One reaction persisted until forty-eight hours, and one did not appear before the forty-eight-hour reading. Both of these subsided completely in another twenty-four hours, leaving no sign except the needle mark. Heise and Brown<sup>6</sup> describe reactions to glycerin broth used in preparing tuberculin; this may be the mech-

TABLE 4. *Pseudoreactions in Tuberculin-Negative Children.*

	DOSAGE	No. OF TESTS
10.0 mg.	O. T.	32
1.0 mg.	O. T.	15
0.1 mg.	O. T.	1
0.01 mg.	O. T. or less	0
Total		48

anism of some of these phenomena, since their occurrence increases with the amount of O.T. used.

It appears that whereas doses smaller than 0.1 mg. may not bring out tuberculin sensitivity or may elicit weak and rather insignificant reactions in positive children, doses stronger than 0.1 mg. call forth an increasing number of rapidly fading pseudoreactions. These possibilities must be borne in mind in interpreting responses to very strong or very weak solutions. Although no absolute rules of interpretation can be made from these observations, they suggest that the presence of even 2 mm. of erythema and induration at seventy-two hours indicates tuberculin sensitivity, especially if the dose employed was 0.01 mg. or less. In other words, the smaller the dose, the more attention is to be paid to faint but persistent reactions; and the larger the dose, the more a dubious reaction is likely to be of no significance, particularly if it begins to fade after the first day. Practically all the unquestionably positive reactions were marked by 1 or 2 cm. of erythema and induration and reached their maximum at forty-eight hours. At that time, the erythema was at its height, and although the induration sometimes became somewhat firmer at seventy-two hours, it was rarely any more extensive in area than before. This observation bears out the figures given by Stewart<sup>7</sup> regarding the growth in area of tuberculin reactions. No reactions beginning to appear later than forty-eight hours were encountered in this study, although a child has been observed in this hospital whose positive response to 0.1 mg. of tuberculin did not appear until the fourth day.

The present study indicates the advantages of the 0.1-mg. test dose, but its potential disadvantages must be considered. Lincoln and Grethmann<sup>8</sup> have recently called attention to the distinctly undesirable activation of disease in and around existing tuberculous foci that may result

from the diagnostic injection of tuberculin. They cite 7 cases in which there was reason to believe that this had occurred. In 2 of these, the dose of tuberculin injected was 0.01, in 1 it was 0.06, in 3 it was 0.1, and in 1 several doses given within twenty-four hours made a total of 0.26 mg. Thus, dangers may be associated with comparatively small, as well as large, doses. No immediate exacerbation of pulmonary or other lesions has been observed to follow tuberculin testing in past years in this clinic, although the usual dose has been 0.1 mg. Nevertheless, a regard for the possibility of such an occurrence has often led to the substitution of weaker doses when strong allergy is suspected, and in the present investigation the proper range for simultaneous tests was established only after the relative sensitivity of the patients had been indicated approximately by previous single tests. However, the patch test was applied to all patients, some of whom (as noted below) responded with marked manifestations at its site, so that many children had simultaneous reactions to that test, as well as to two and occasionally three of the intradermal inoculations. There were no evidences of unfavorable activation around tuberculous foci. Thus, although agreeing that caution is necessary in the use of tuberculin, we believe that experience allows the recommendation of 0.1 mg. of old tuberculin as a routine dose for the Mantoux test on young patients such as those in this clinic. The use of smaller amounts is suggested for patients suspected of skeletal or lymph-node tuberculosis, pleural effusion, phlyctenular keratitis and erythema nodosum, for those with a history of long exposure to the disease, and for persons above twelve years of age. In passing, it may be mentioned that the degree of tuberculin sensitivity to the graded and measured tests in this investigation showed no relation to the extent or seriousness of the tuberculous process.

The Patch Test

Vollmer and Goldberger,<sup>9</sup> in 1937, introduced the application to the skin of filter-paper squares soaked with pure O.T. as a test of tuberculin sensitivity. The case of this technic, for both physician and patient, aroused immediate interest, and the relative accuracy of the method has been indicated by several published studies recently summarized by Vollmer.<sup>10</sup> With one outstanding exception, the agreement between the patch and the Mantoux reactions has been quite close.

In the study here reported, 336 infants and children were tested with simultaneous patch and Mantoux tests. As shown in Table 5, no patient who failed to react to the Mantoux test gave any

reaction to the patch, so that the latter test cannot be suspected of producing false positive results, nor did it bring to light positive reactors not discovered by intradermal testing. In 113 children, there were positive reactions to both tests; among this group were several cases in which the weaker intradermal doses brought forth no response. Of the 6 patients in whom the two tests disagreed, 3 reacted only to comparatively strong intradermal doses. Thus, in this study, patients responded to the patch tests in nearly the same degree as to the 0.1 mg. intradermal doses. Apparently, except in rare cases, the patch makes a suitable screening test and would be highly efficient if followed, when negative, by a strong intradermal inoculation, such as the introduction of 10 mg. of OT.

As others have observed, an occasional unpleasantly large and uncomfortable reaction to the patch test was noted, and here again the mani-

TABLE 5 Comparison of Patch and Intradermal Tests

RESULT OF PATCH TEST	RESULT OF INTRADERMAL TEST	NO. OF CASES
Negative	Negative (all doses)	217
Positive	Positive (any dose)	113
Negative	Positive (0.1 mg.)	3
Negative	Positive (1.0 mg.)	2
Negative	Positive (10.0 mg.)	1

festations at the sites of the patch and intradermal tests ran roughly parallel. Although the actual patches of filter paper impregnated with tuberculin are only 1 square cm. in area, each of these occasionally called forth an induration of 3 cm. or more in diameter, with vesiculation and, at times, shallow ulceration. Since two such squares are present on each strip of adhesive (on either side of a control square of plain filter paper), the reactions may coalesce into a large single area. Besides these situations, it was noted that the children often spoke of itching at the patch-test sites, although there was seldom any complaint from the intradermal reactions. Vollmer<sup>10</sup> has pointed out the possibility of avoiding severe reactions by using weaker tuberculin solutions in the manufacture of the patches or, more simply, by leaving them in contact with the skin a shorter time.\*

\*We have made a few observations using transparent Scotch cellulose tape instead of adhesive and suggest it as a satisfactory backing for the test patches. The immediate surroundings of the impregnated filter paper squares can be kept under observation at the earliest sign of redness seen through the transparent tape, the whole strip can be removed. This is suggested as a means of avoiding unnecessarily prolonged application of tuberculin to the skin of very sensitive subjects.

## SUMMARY AND CONCLUSIONS

Simultaneous intradermal (Mantoux) tests with graded doses of O.T. (old tuberculin) were performed on 336 infants and children under thirteen years of age. The same patients were also tested by the patch method.

Test doses of less than 0.1 mg. were less than 85 per cent as accurate as those of 0.1 mg. in revealing tuberculin sensitivity. Doses of 0.1 mg. were 97 per cent as accurate as those above that amount.

Weak positive or questionable reactions in patients with actual tuberculin allergy were usually noted in weak test doses. These reactions were characterized by a tendency to persist as mild manifestations at the site of inoculation for three or four days.

False positive reactions or pseudoreactions in patients seemingly without tuberculin allergy were the results of strong doses and may have been brought about by sensitivity to the broth. These were characterized by widespread erythema at twenty-four hours but almost complete disappearance at forty-eight.

Since the minimum number of doubtful responses was obtained with 0.1 mg. of OT, and since this dose is only slightly, if at all, more liable to induce undesirable perifocal reactions than weaker tests are, it seems to be the most suitable amount for a routine intradermal test of clinic children in the vicinity of Boston.

The tuberculin patch test was positive in 113 (97 per cent) of 116 children who reacted to 0.1 mg. or less of O.T. by the intradermal method.

No correlation between tuberculin sensitivity and degree of infection was apparent.

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## MEDICAL PROGRESS

### THE ENCEPHALITIDES OF VIRUS ETIOLOGY\*

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THE largest epidemic of encephalitis of known etiology that has hitherto been reported occurred during the past summer and fall.<sup>1</sup> Approximately 3000 persons were affected in an area encompassing the north central states and Canadian provinces. This outbreak, however, did not appear without forewarning. During the last ten years, similar but less extensive outbreaks have occurred in the Midwest,<sup>2-8</sup> as well as in the East<sup>9, 10</sup> and Far West.<sup>11-18</sup> The most recent epidemic appears now to be merely a higher peak in a series of recurrent waves. The clinical aspects of the disease during these outbreaks have been very similar, but have also been distinctly different from those associated with the older type of encephalitis, which appeared in 1916 and has been variously termed "epidemic encephalitis," "encephalitis lethargica" and "von Economo's disease,"<sup>19</sup> and the etiology of which is unknown. In the recent outbreaks, three distinct etiologic agents, all viruses, have been demonstrated. Newer developments in laboratory technic have now made it possible to identify them, to trace their distribution, and to relate them to a given outbreak. These subjects will be discussed in this report, together with a brief review of the clinical manifestations of these diseases and their treatment and prevention.

#### ETIOLOGY, OCCURRENCE AND DISTRIBUTION

Much confusion has existed in the past, and still exists, regarding the diagnosis of encephalitis. Thus, Wilson,<sup>20</sup> in a chapter on epidemic encephalitis, discusses encephalitis lethargica, Japanese B encephalitis and St. Louis encephalitis, with the implication that they are but variants of the same basic disease. Literally, the word encephalitis means "inflammation of the brain." It has been used loosely to characterize a number of clinical

syndromes, — in themselves not too definite, — regardless of etiology. These clinical pictures may be produced by a variety of agents: bacteria, parasites, toxins, chemicals, viruses and, presumably, others as yet unknown. Difficulty in diagnosis and classification is almost certain to exist until the etiology of the various types of encephalitis is determined, and until the clinical criteria for diagnosis are carefully re-evaluated in the light of the etiology. Similar confusion has existed with other morbid states: pneumonia, for example, may be produced by oils (lipoid pneumonia), gases, dusts, a variety of bacteria and viruses.

During the last fifteen years, the discovery of a number of viruses affecting the central nervous system has helped to clarify the problem of encephalitis, and has permitted more or less detailed, although tentative, classifications on an etiologic basis.<sup>21-28</sup> For practical clinical purposes, the encephalitides of man may be divided into three groups:

- Group I. Bacteria, protozoa and other parasites
- Group II. Viruses
  - St. Louis encephalitis
  - Equine encephalomyelitis (Eastern and Western types)
  - Japanese B encephalitis
  - Australian X disease
  - "Forest-spring" encephalitis of Russia
  - Lymphocytic choriomeningitis
  - Louping ill
  - Virus B
  - Poliomyelitis
  - Rabies
- Group III. Etiology unknown, possibly virus
  - Encephalitis lethargica (von Economo's disease)

A number of other conditions are sometimes included in classifications of encephalitis, namely, postinfection encephalitis, postvaccinal encephalitis, postrabic-treatment encephalitis, the large group of primary demyelinating diseases and a miscellaneous group of degenerative processes caused by chemicals, toxins and so forth. No useful function would be served by including these encephalopathies in the above classification, although they must be kept in mind in differential diagnosis.

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Of these three subdivisions, only those due to specific viruses (Group II) are concerned here. Since poliomyelitis and rabies constitute special and rather well defined problems,<sup>29-30</sup> they will not be considered further.

Only two types of virus encephalitis, other than poliomyelitis, have thus far occurred in significant epidemics in this country. These are St. Louis encephalitis and equine encephalomyelitis. Other forms have occurred either sporadically, such as rabies and lymphocytic choriomeningitis, or as a result of laboratory infections, such as louping-ill and virus B. Japanese B encephalitis, Australian X disease and 'forest spring' encephalitis of Russia have been epidemic in their respective countries, but have not been seen and recognized in the Western Hemisphere.

### *St. Louis Encephalitis*

In the late summer of 1932, 38 cases of an unusual type of encephalitis occurred in Paris, Illinois.<sup>31</sup> No etiologic diagnosis was made. The following summer, however, more than 1000 cases of a similar disease occurred during August, September and October in and about St. Louis and Kansas City.<sup>32-34</sup> Cases of some kind of encephalitis, possibly the same disease, had existed in this area prior to the 1933 outbreak, since in the St. Louis Children's Hospital sporadic encephalitis had shown a seasonal distribution, with a peak in July and August, during the previous fourteen year period. In any event, a virus pathogenic for monkeys and mice was isolated in 1933 from several fatal cases<sup>31-34</sup> and was shown by almost all investigators<sup>32-39</sup> to be a new different and specific agent. This was the first outbreak of acute encephalitis in this country in which a virus was definitely established as the etiologic agent.<sup>40</sup>

It was found that serums from patients who had recovered from the disease contained substances that would specifically neutralize or prevent the development of infection in animals otherwise susceptible to the St. Louis virus.<sup>32</sup> This test therefore provided a method of determining what persons had been infected with the virus, either acutely or subclinically as well as the geographic distribution of the disease. Thus, in the St. Louis area it was found that serums of about 90 per cent of the convalescents and about one fifth of the 'normal controls' who had not been ill contained neutralizing substances, whereas such antibodies were not found in the serums of patients with typical encephalitis lethargica (von Economo's disease), poliomyelitis and postinfectious encephalitis.<sup>41-44</sup> Furthermore, serologic evidence indicated that the virus was not confined to the St. Louis area but had presumably caused the

outbreak in Paris, Illinois, as well as sporadic cases in New York City and the central and western states. Since 1933, repeated outbreaks have occurred in the Midwest and Far West, with apparently increasing frequency and size, and widening geographic distribution.<sup>7-11, 15, 17, 18, 44-47</sup> A significant factor in this process may have been the migration of labor populations from the Dust Bowl to the Far West.<sup>48</sup> During the last three years, cases apparently due to the virus of either St. Louis encephalitis or the Western type of equine encephalomyelitis, or both, have occurred in the same outbreaks.<sup>6-10, 15, 17, 18</sup> With the exception of the 2 patients in New York City, no proved cases of St. Louis encephalitis have been reported from the Atlantic Seaboard.

### *Equine Encephalomyelitis*

Until 1938, equine encephalomyelitis was considered to be primarily a disease of horses. Although the infection had probably existed on this continent for a number of years, it was first identified as a distinct entity by the isolation of the virus from horses during the 1930 epizootic in the San Joaquin Valley in California.<sup>49</sup> During 1931 the disease was recognized in horses throughout California, in Oregon and in Nevada.<sup>50</sup> In 1933, another virus was isolated from horses in the eastern section of the United States.<sup>1, 5</sup> These two strains of virus were found to be immunologically distinct and to differ from other known viruses.<sup>6, 51-53</sup> They have since been known as the Western and Eastern strains of the virus or equine encephalomyelitis. By the end of 1937, the disease was reported in all sections of the United States except New England,<sup>54-60</sup> and a similar disease was reported from Mexico.<sup>61</sup> In 1938, extensive outbreaks occurred in thirty-nine of the forty-eight states, including New England,<sup>62</sup> and a third, distinct strain of virus was identified in Venezuela.<sup>64</sup> Since then, the disease has occurred in horses throughout the country.<sup>65</sup> Curiously enough, the western and eastern varieties of the virus have shown until recently a sharp geographic delimitation in distribution, the Appalachian Mountains providing the boundary. Both types have now been isolated in Alabama, however, and the Eastern strain has been found in Texas.<sup>66</sup>

The history of the recognition and apparent spread of human encephalitis due to the viruses of equine encephalomyelitis is similar to that of the disease in horses. In 1931, in California Meyer<sup>67</sup> encountered 3 human cases with pathologic lesions similar to those found in horses, although the virus was not isolated and neutralizing antibodies were not demonstrated. During the next six years,

there was no record of outbreaks in man, although the viruses were widespread, as indicated by the occurrence of the disease in horses. There was some suggestion that sporadic cases occurred during this period.<sup>65, 69</sup> In the summers of 1937 and 1938, however, outbreaks of encephalitis occurred in California, North Dakota, Minnesota, Saskatchewan and Massachusetts, and an etiologic diagnosis was established by the isolation of both types of the equine virus and demonstration of specific neutralizing substances in the serums of patients.<sup>5-8, 12, 48, 70-75</sup> The epidemic in Massachusetts was due to the Eastern variety of virus; all the others were due to the Western type. One strain of the Eastern virus isolated from a fatal human case produced typical encephalomyelitis in the horse.<sup>76</sup>

During the last three summers, no epidemics have occurred in the East, but outbreaks of increasing severity have been reported in the Midwest and Far West,<sup>15, 17, 18</sup> culminating in the extensive outbreak during the past summer in the north central states and the adjoining provinces of Canada.<sup>1</sup> As pointed out above, both the Western equine and St. Louis viruses have been isolated in California, Colorado, North Dakota and Washington.<sup>7, 14, 15, 17, 18, 68, 77</sup> Thus far, the evidence indicates that the recent epidemic in the Dakotas and surrounding states and in Canada is due to the Western strain of equine virus,<sup>78-80</sup> although poliomyelitis probably coexists in certain areas. Sporadic subclinical and fatal infections have been reported in laboratory workers.<sup>81-83</sup>

#### *Other Types of Encephalitis*

Three other specific types of acute encephalitis have occurred in epidemic form, namely, Japanese B encephalitis, Australian X disease and the "forest-spring" encephalitis of Russia.

The Japanese disease has been recognized since 1871.<sup>84, 85</sup> It is caused by a specific virus,<sup>35, 38, 86, 87</sup> which is apparently related antigenically to, although not identical with, the St. Louis virus.<sup>38, 88-90</sup>

Australian X disease, or the so-called "mysterious disease," occurred in New South Wales in 1917 and 1918 and returned in milder form in 1922 and 1926.<sup>91-94</sup> It has not been seen since. Enough evidence was obtained, however, to show that the infectious agent was probably a virus, although the strain has been lost so that comparison with the other viruses in this group has been impossible.

Recent reports<sup>95-98</sup> have described a seasonal encephalitis that has existed in Russia for at least twenty-five years. It occurs in the spring, attacks

primarily men laboring in the forest, and accordingly is known as "forest-spring" encephalitis. The etiologic agent is a virus that is distinct from that of St. Louis encephalitis but is antigenically related to the virus of Japanese B encephalitis. Differentiation is possible, however, by immunologic methods.

The virus of louping ill, under natural conditions, produces an encephalitis of sheep in Scotland, where no epidemics or even sporadic cases in man have been reported, although accidental laboratory infections have occurred.<sup>99</sup> The disease is of chief interest academically because of the similarity of the experimental infection to that produced by other viruses causing acute encephalitis.

The B virus was isolated from the central nervous system and spleen of a laboratory worker who had developed an acute ascending myelitis following the bite of a monkey.<sup>100, 101</sup> Apart from such accidental infection, this disease is unknown in man.

Lymphocytic choriomeningitis, a natural disease of mice, occurs sporadically in man.<sup>102-105</sup> The specific virus has been isolated from patients. The disease appears to be primarily a meningitis, but because of the lack of pathological data, the extent of involvement of the central nervous system in man is unknown.

#### TRANSMISSION AND HOST RESERVOIRS

The source and manner of spread of the viruses causing encephalitis in man presented a puzzling problem that has tested the ingenuity and imagination of a large number of investigators. Even in the earliest outbreaks, it became evident that individual contact did not explain the occurrence and spread of the infections. Certain aspects of the epidemics—seasonal occurrence, geographic distribution and related outbreaks in animals—suggested animal and avian host reservoirs and vector transmission. During the last few years, this concept has been substantiated to a considerable degree. In fact, for only two of the known virus encephalitides—poliomyelitis and Australian X disease—is evidence of potential animal reservoirs lacking, and vector transmission is possible with at least five of the viruses.

This advance has been achieved by the correlation of several types of data obtained by studying the following: the epidemiology; the susceptibility of domestic and wild animals and birds; the distribution of the virus in blood and tissues of experimentally or naturally infected animals and birds; the isolation of the virus from naturally infected animals and birds; the presence of neutralizing substances in the blood of

man and of wild and domestic animals and birds; the experimental transmission by vectors; and the isolation of the virus from naturally infected vectors and the transmission of disease by them to normal susceptible animals.

### *St. Louis Encephalitis*

Studies of the 1933 outbreak in St. Louis did not reveal the mode of transmission,<sup>3, 4</sup> although, on reanalyzing the data, Casey and Broun<sup>100</sup> came to the conclusion that every known feature was common to that of a mosquito-borne disease. Although the virus was found only in the central nervous system of fatal cases,<sup>31</sup> it has been demonstrated in the blood of experimental animals.<sup>107</sup> Infection could be produced by intranasal inoculation, as well as by direct intracerebral injection.<sup>32</sup> Clinical signs of infection occurred in monkeys and mice, and possibly in mules,<sup>4</sup> but the other common laboratory animals were resistant. The virus was not found in mosquitoes collected in epidemic areas.<sup>3</sup> One species of anopheline mosquito became infected by biting a diseased animal,<sup>108</sup> but transmission was not accomplished.

Additional information then followed rapidly. The fact that mice could apparently be immunized by intranasal instillation of nasopharyngeal washings from patients<sup>109</sup> suggested that subinfective amounts of virus were present in the nasal secretions and that contact infection might therefore be possible. Wild mice were found to be susceptible,<sup>110</sup> and adult mice contracted the disease by eating infected, newly-born mice, suggesting a possible mode of transmission in nature.<sup>111</sup> The common mosquito, *Culex pipiens*, was able to take up the virus but not to transmit it.<sup>112</sup> Certain individual field and meadow mice were found to be susceptible to the St. Louis virus, whereas others were resistant<sup>113</sup>; this suggested that the latter had acquired immunity from natural infection or were carriers and hence potential reservoirs of the virus.

Because the serums of a significant number of wild and domestic animals and birds were found to be capable of neutralizing the St. Louis virus,<sup>17, 18, 114</sup> the possibility of previous infection was indicated. Inoculation of St. Louis virus intracerebrally into horses whose serums contained neutralizing antibodies resulted in no apparent illness, whereas animals whose serums did not contain antibodies developed an acute encephalitis, indistinguishable from that produced by the virus of equine encephalomyelitis.<sup>115</sup> During the course of this experimental disease, the infective agent was found in the nasal secretions but could not be detected in the blood. It seems unlikely, therefore, that transmission from the horse could be

accomplished by blood-sucking insects. Since the virus is present in nasal secretions, transmission by contact or by mechanical vectors may be possible, with the nasopharynx as the portal of entry.

Finally, Hammon and his co-workers<sup>110</sup> reported the isolation of St. Louis virus from mosquitoes (*C. tarsalis*) collected from areas in which human encephalitis occurred. This insect may therefore be the vector, and several species of wild and domestic birds and mammals may be the host reservoirs; both horses and human beings may be only accidental victims. It remains to be determined, however, whether the virus is actually present in the blood of these animals and birds, whether it can be transmitted from them to susceptible hosts by mosquitoes, and whether or not contact produces infection. Until such data are available, the epidemiology of this disease will remain incomplete.

### *Equine Encephalomyelitis*

Soon after the recognition of epidemics of equine encephalitis in horses, it was noted that the disease disappeared in the fall shortly after the first frost, which suggested the possibility that an insect vector might be involved. This suspicion was strengthened by Kelser's demonstration,<sup>117</sup> amply confirmed by others,<sup>118-124</sup> of the experimental transmission of the disease in the laboratory by mosquitoes. Studies of both the Western and Eastern strains of virus by many investigators<sup>125-142</sup> revealed the wide range of infectivity of the agents for animals and birds by several routes of infection. Furthermore, the virus could be detected in their bloods in the early stages of the disease.

On the basis of the epidemiology of the disease in horses in the eastern United States, TenBroeck, Hurst and Traub<sup>143</sup> considered birds as possible host reservoirs. This hypothesis was supported during the 1938 epidemic in the East by the isolation of the virus from the ring-necked pheasant<sup>144, 145</sup> and the pigeon,<sup>146</sup> and recently in the West from the prairie chicken.<sup>78</sup> Mosquitoes capable of transmitting the infection existed in these areas,<sup>1, 124, 147</sup> but numerous attempts to isolate the virus from mosquitoes collected during epidemic periods failed. More recently, however, neutralizing antibodies for the Western strain of equine virus were found in the serums of a number of wild and domestic birds and mammals in epidemic areas in the West,<sup>144</sup> and the virus was isolated from mosquitoes (*C. tarsalis*) collected in these areas.<sup>110</sup> Thus, it seems probable that mosquitoes are important vectors in transmitting equine encephalomyelitis among birds and ani-

mals, the primary hosts, as well as to man, a secondary host.

Outbreaks have been recorded, however, in an area that had been dry for months and absolutely free from mosquitoes for weeks before the appearance of the disease.<sup>8</sup> It is entirely possible that arthropod vectors, such as the tick, may be involved.<sup>148, 149</sup> Moreover, the Western strain of equine virus has recently been isolated from naturally infected *Triatoma sanguisuga*, commonly known as the assassin bug or the bloodsucking cone nose, and in one case the disease has been transmitted to guinea pigs<sup>150</sup> by this arthropod.

### Other Types of Encephalitis

Considerable information is available regarding the host reservoirs and mode of transmission of certain other encephalitides of virus etiology. Japanese B encephalitis can be transmitted by mosquitoes (*C. pipiens*), but host reservoirs are not known, although monkeys, mice and sheep are susceptible to the virus.<sup>38, 85, 86, 88, 90, 151, 152</sup> The virus of the "forest-spring" encephalitis of Russia has been isolated from rodents in endemic areas and can be transmitted by ticks.<sup>95-98</sup> Little is known regarding Australian X disease except that the monkey, sheep, horse, calf and possibly guinea pig were shown to be susceptible. Louping ill is primarily a disease of sheep and is transmitted by the sheep tick, *Ixodes ricinus*.<sup>153</sup> No vectors are known for virus B encephalitis, which presumably is a disease of monkeys.<sup>100, 101</sup> Lymphocytic choriomeningitis is a natural disease of mice, but the virus has also been isolated from guinea pigs, monkeys and dogs, as well as from man,<sup>154</sup> and laboratory transmission has been effected by mosquitoes.<sup>155</sup>

### CLINICAL AND PATHOLOGICAL ASPECTS AND DIAGNOSIS

The acute encephalitides of virus etiology that occur epidemically are remarkably similar in their clinical aspects, so that in the present state of knowledge differentiation between them on this basis is not possible, except in cases of poliomyelitis.

St. Louis encephalitis<sup>4, 18, 47, 156-158</sup> and the Eastern<sup>9, 70, 73, 74</sup> and Western<sup>1, 5, 7, 14, 15, 18, 68, 77, 82, 83, 159</sup> types of equine encephalomyelitis have occurred epidemically in man in this country. Each of these diseases has appeared in midsummer or late summer. The onset of illness was usually abrupt, although in some patients a prodromal period occurred, characterized by a grippe-like syndrome of fever, malaise, muscle pains and so forth. Headache, fever, mental confusion and

signs of meningeal irritation were outstanding features. In severe cases, drowsiness, tremors, convulsions and coma occurred early in the course, particularly in the younger age group. Jaundice was apparent in some cases.<sup>18</sup> Signs of involvement of the central nervous system varied considerably. Some showed only hyperactive reflexes, whereas others developed extensive paralyses which were usually spastic. Ocular manifestations were rare. The acute illness usually subsided in one or two weeks, and the majority of deaths occurred within the first week. Sequelae were rare in patients who recovered from St. Louis encephalitis,<sup>157</sup> but were frequent and often severe in those—particularly children—surviving equine encephalomyelitis.<sup>68, 74, 77</sup> The mortality was much higher with the Eastern type of equine encephalomyelitis than with either the Western or St. Louis type, which is in keeping with the greater virulence of the Eastern strain of equine virus.

Examination of the cerebrospinal fluid revealed elevated protein, normal sugar and a pleocytosis varying from 10 to 2000 cells per cubic millimeter. In general, the cell counts were lower, 50 to 250, and mononuclear cells predominated with St. Louis encephalitis, whereas the total counts were higher and polymorphonuclear cells predominated in the early stages with equine encephalomyelitis. Polymorphonuclear leukocytosis was found in the blood of some patients.

The pathologic changes in each of these varieties of encephalitis were localized chiefly in the central nervous system and were essentially similar.<sup>7, 73, 71, 160-162</sup> Edema, congestion, cellular infiltration about vessels and in the parenchyma, neuronal degeneration and neuronophagia were present. The process was diffuse, although the spinal cord was usually spared. Considerable parenchymal infiltration with polymorphonuclear leukocytes, arteritis and thrombosis of small arteries and arterioles were found in the brain and brain stem of fatal cases due to the Eastern strain of equine virus.<sup>162</sup>

Differential diagnosis is often difficult,<sup>163</sup> particularly in sporadic cases,<sup>164</sup> and a final etiologic diagnosis must be made with laboratory aid (Table 1). The Western strain of equine virus has been found in the blood<sup>8, 75</sup> and cerebrospinal fluid<sup>82</sup> early in the course of this disease. Each of the viruses has been isolated from the nervous tissue of fatal cases.<sup>70-72, 78</sup> Animals are usually employed for this purpose, although tissue culture may be a more sensitive method.<sup>165</sup> An etiologic diagnosis may also be made by the demonstration of neutralizing or complement-fixing antibodies in serums<sup>27, 79, 80, 166, 167</sup> or cerebrospinal fluid from

convalescents<sup>107</sup> Neutralizing antibodies may be detected by the end of the first week after onset in some cases,<sup>26 107</sup> but more frequently during the second and third weeks. The most reliable evidence is obtained when serums taken during the acute and convalescent stages show an increase in titer.

As mentioned earlier, encephalitis lethargica or von Economo's disease was a fairly definite clinical syndrome, which differed in many respects from the acute encephalitides just described. Following its appearance in 1916, the disease increased

progressed for years, with remissions and relapses. The pathologic changes were inflammatory in nature and most prominent in the area of the basal ganglia. The presence of varying stages of inflammation and nerve cell degeneration suggested persistence of an active process late in the course of the disease.<sup>108 109</sup> The etiology was not established, in spite of extensive investigation, and it is therefore not possible to classify this syndrome as a virus disease.

Lymphocytic choriomeningitis is characterized chiefly by the signs and symptoms of meningeal

TABLE 1 *Certain Differential Features of the Encephalitides Occurring in Man in the United States*

TYPE OF ENCEPHALITIS	SEASON	AGE	ONSET	COURSE	SEQUELAS	APPROXIMATE MORTALITY %	CEREBROSPINAL FLUID		PRESENCE OF SPECIFIC VIRUS		CENTRAL NERVOUS SYSTEM	PRESENCE OF CIRCULATING ANTIBODIES
							WHITE CELL COUNT	PREDOMINATING CELLS	BLOOD	CEREBROSPINAL FLUID		
St. Louis	Late summer	Adults	Sudden	Acute	Rare	20	10-1000	Mononuclear	?	?	+	+
Eastern equine	Late summer	Children	Sudden	Acute	Frequent and severe	0	70-7000	Polymorphonuclear early mononuclear late	?	?	+	+
Western equine	Late summer	Any	Sudden	Acute	Frequent and severe	20	100-1000	Polymorphonuclear early mononuclear late	+	+	+	+
Encephalitis lethargica	Winter	Any	Sudden gradual or not apparent	Chronic	Frequent and progressive	30	0-100	Mononuclear	0	0	0	0
Lymphocytic choriomeningitis	Any	Any	Sudden	Acute	Very rare	0	100-5000	Lymphocytes	+	+	?	+

to epidemic proportions, reaching a peak in 1924 and 1925 and declining during the next few years. New cases have been comparatively rare during the last decade. This form of the disease occurred in the winter and affected all age groups. The onset of acute symptoms and signs was sudden in some cases, gradual in others, and at times was unrecognized until the appearance of sequelae. Low grade fever, minimal evidences of meningeal irritation, headache and, occasionally, somnolence were the chief early manifestations. The cerebrospinal fluid showed minimal changes—slight increase in protein and a count of 10 to 50 mononuclear cells—or none at all. The illness was ordinarily chronic and gradually progressive. Ocular paralysis, somnolence or drowsiness, emotional changes and, sometimes, paralysis occurred during the succeeding weeks and months. Emotional and mental deterioration and Parkinson's syndrome were usually characteristic features. In some cases, complete recovery occurred, in others, the disease

irritation, although drowsiness and coma may occur. Other conditions that must be considered in differential diagnosis are acute meningitis, chronic meningitis (tuberculous and syphilitic), the post-infection encephalitides and other demyelinating processes.

### TREATMENT

Treatment of all the encephalitides is chiefly symptomatic at present. Lumbar puncture and the intravenous administration of hypertonic dextrose solutions are of value in relieving increased intracranial pressure. Sedation and correction of dehydration should be carried out when indicated. Chemotherapy with sulfonamides is of no value, except for the prevention or treatment of complications, such as bronchopneumonia.

Specific antiserum has been employed in horses and experimental animals, with conflicting results.<sup>110 112</sup> Convalescent human serum was of no demonstrable therapeutic value during the St.

Louis epidemic.<sup>173</sup> As Hammon<sup>18</sup> has pointed out, specific therapeutic antisera are of no avail at the present time because a sufficiently early etiologic diagnosis cannot be made. Rosenow and his co-workers<sup>4, 174</sup> have reported studies indicating that streptococci are etiologic agents of the various types of encephalitis. On the basis of this work, they have advocated antistreptococcus serum and streptococcal vaccines for therapy and prophylaxis. Their results have not been confirmed by other investigators.<sup>4</sup>

### PREVENTION

Three methods of attack now appear to be applicable to the prevention of epidemics of encephalitis in this country: extermination of host reservoirs, extermination of vectors and immunization of susceptible hosts. The evidence now available indicates that the natural reservoirs may be so widely diverse in animals and birds<sup>78, 111, 141-146</sup> as to make their extinction impossible. Measures to control mosquitoes and other insects are feasible in many populated areas of the country, and should be carried out where applicable. Immunity to equine encephalomyelitis can be produced in susceptible hosts by vaccines containing the specific virus, which has been killed by formalin or ultraviolet light.<sup>175-179</sup> Such vaccines have been used in horses, with apparently good results.<sup>63, 65, 179</sup> Purified vaccine<sup>180-182</sup> is now available and has been employed in human beings with only minor reactions.<sup>183, 184</sup> Its use seems to be desirable in laboratory workers and in those persons in endemic areas whose occupations offer frequent opportunity for infection. Animals have been immunized against St. Louis encephalitis virus by the use of living virus,<sup>185, 186</sup> but vaccines that can safely be used in man are not yet available.

Further investigation of the problems of prevention is essential, because of the military activities and concentration of men in training camps situated in endemic areas.

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CASE RECORDS OF THE  
MASSACHUSETTS GENERAL HOSPITALANTE MORTEM AND POST MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C CABOT

TRACY B. MALLORY, M.D., Editor

## CASE 27521

## PRESENTATION OF CASE

*First admission.* A thirty-year old Italian housewife was admitted to the hospital because of swelling of the legs and abdomen for three weeks.

About six years before entry, the patient had a slight sore throat, followed shortly by painful swelling of her joints. She remained in bed for three months, because a local physician thought "her heart was affected." Her tonsils were removed, and she remained well until four years before entry when again she had "rheumatism," and stayed in bed for two or three months. At this time, some abscessed teeth were found and removed. Following this illness, there was insidious onset of shortness of breath. Dependent edema appeared about eight months before entry, and was not relieved by theocin, which was given by the patient's physician.

Her past and family histories were not of importance. She had an eight-year old son.

On examination, the patient appeared well developed but poorly nourished; she was markedly dyspneic, with cold extremities and circumoral cyanosis. The neck veins were distended. The heart was enlarged 4 cm to the right and 12 cm. to the left of the midline, and fibrillated at a rate of about 156, only about half the beats coming through at the wrist. There was a prominent precordial heave, and a diffuse systolic murmur at the apex, with a mid diastolic murmur and thrill. Each lung field exhibited basal rales. The liver border was tender, and lay three finger breadths below the costal margin. Free fluid was present in the lower abdomen, and the sacral tissues and lower extremities were quite edematous.

The temperature was 97°F, the pulse 92, and the respirations 25.

Examination of the blood showed a red cell count of 6,010,000 with 90 per cent hemoglobin, and a white-cell count of 7400 with 62 per cent polymorphonuclears. The blood Hinton reaction was negative. The urine showed a slight trace of albumin, and contained many hyaline casts and a few white blood cells per high-power field. An electrocardiogram confirmed the diagnosis of

auricular fibrillation, and demonstrated prominent right-axis deviation, with inversion of T waves in Leads 2 and 3. The vital capacity was 1200 cc. The basal metabolic rate was -16 per cent.

The patient was given diuretics and Southey tubes, with improvement in her condition. In the fourth hospital week, total thyroidectomy was performed. Tetany developed after the operation, the blood calcium falling to 8 mg., and the blood phosphorus rising to 6 mg. per 100 cc. Following recovery, the patient was discharged at the end of the second hospital month on digitalis and calcium chloride. By this time, the basal metabolic rate had fallen to -21 per cent, the vital capacity had improved to 1450 cc., and the pulse had become regular at 70.

*Second admission* (one year later). The patient was readmitted because of pain in the back and because of recurrence of her dyspnea and edema. She had remained in bed on digitalis. Nine hours before reentry, she experienced a sudden, sharp pain in her left flank and soon afterward passed a small amount of bloody urine. She was found to be in congestive failure, the condition being little changed from that observed on the first entry, except for the presence of hematuria, which persisted throughout the two weeks of her hospital stay, and except for slight evidence of hypothyroidism—dry skin, a basal metabolic rate of -27 per cent, a blood pressure of 110 systolic, 93 diastolic, and a pulse of 60. The nonprotein nitrogen was 47 mg. per 100 cc. Three and a half liters of dark yellow ascitic fluid was removed by tap. The patient was given Salyrgan and discharged improved.

*Third admission* (four months later). The patient was readmitted with her usual complaints of dyspnea and edema, to be discharged two weeks later after the usual diuresis. The heart rhythm was regular, and the urine was normal except for the presence of albumin.

*Fourth admission* (three and a half years later). During the preceding four years, the patient had been able to do light housework, remaining fairly well until two and a half months before readmission. She then had a cold, accompanied by pain in the chest and migratory swelling of the fingers, shoulders and knees. After a week, the dyspnea, orthopnea and edema reappeared. Re-examination showed a rumbling apical diastolic murmur in addition to the old systolic murmur. The heart was again in fibrillation, and the blood pressure had risen to 115 systolic, 70 diastolic. The white cell count ranged from 13,000 to 15,000, with 76 per cent polymorphonuclears. The sedimentation rate was elevated to 15. The blood

calcium was 9.8 mg., and the blood phosphorus 5.3 mg. per 100 cc. The urine showed a ++++ test for albumin and contained many white blood cells, with a few casts and red blood cells per high-power field. On discharge, after two months of bed rest, there were persistent signs of active disease in the joints.

*Fifth admission* (six months later). The patient returned to the hospital because of a return of congestive failure. She was discharged improved, after a month.

*Sixth admission* (four months later). The patient was once more admitted because of decompensation. The basal metabolic rate had risen to normal. The calcium and phosphorus levels of the blood were each 7.1 mg. per 100 cc. She was given AT-10 (the calcinosis factor of previtamin D), and elevation of the blood-calcium level to 12 mg. per 100 cc. was attained. A colon-bacillus infection of the urine was discovered and treated satisfactorily with mandelic acid.

*Seventh admission* (two weeks later). The patient received the usual treatment for recurrent decompensation, to be discharged after a month.

*Eighth admission* (fifteen months later). The patient was hospitalized for a day because of "numbness" in the hands and face, and a "tight feeling" in the abdomen. The Chvostek and Trousseau signs were markedly positive, and she appeared to be in incipient tetany. The symptoms were relieved by an increase in the daily ration of calcium lactate.

*Final admission* (one month later — seven and a half years after her initial entry). The patient was readmitted because of progressive dyspnea. She had been leading a bed-chair existence. Two days before entry, she began to have considerable pain in the abdomen.

On examination, she appeared acutely ill, severely dyspneic and orthopneic, and quite cyanotic. The heart was enormous, beating irregularly in slow, coupled rhythm. Murmurs were present as before. Rales extended half way to the angle of the scapula on the right. The liver was several centimeters below the level of the umbilicus and was acutely tender. There was little peripheral edema.

The temperature was 99°F., the pulse 40, and the respirations 18. The blood pressure was 120 systolic, 70 diastolic.

Examination of the blood showed an elevation of the white-cell count to 15,400. The blood calcium was 8 mg., and the phosphorus 14 mg. per 100 cc. Other laboratory studies were much as before.

The temperature rose to 101.2°F., and the pulse to 100. Death occurred suddenly and unexpectedly on the third hospital day.

#### DIFFERENTIAL DIAGNOSIS

DR. RICHARD J. CLARK: This patient was quite evidently one of that group subjected to total thyroidectomy for the treatment of heart failure a few years ago. Six years before the first admission, she had acute rheumatic fever, with cardiac involvement aggravated by a second bout of infection two years later, when she first showed symptoms of congestive heart failure that progressed up to her entry into the hospital. At entry, she was in acute congestive failure, with cardiac enlargement and auricular fibrillation. She showed evidence of mitral damage, with an apical systolic and mid-diastolic murmur and thrill. The electrocardiogram at entry was consistent with mitral disease and right ventricular hypertrophy. The temperature and white-cell count afforded no evidence of active rheumatic infection at this time. The findings in the urine were consistent with those of congestive heart failure.

The patient's condition improved with diuretics and Southey tubes. Although the basal metabolic rate was -16 per cent, a total thyroidectomy was performed. This must have been one of the early cases in the series, because later it was believed that the presence of an initially low basal metabolic rate gives a relatively poorer outlook for improvement with this type of therapy. The patient developed clinical and laboratory evidence of hypoparathyroidism after the operation, but otherwise made a good convalescence. I note that four weeks after total thyroidectomy the basal metabolic rate had fallen only to -21 per cent, which is not much of a drop from the preoperative rate of -16.

One year later, the patient re-entered the hospital with recurring congestive failure and also pain in the left flank followed by bloody urine. Evidently she had experienced what is not uncommon in the disease complex — a renal infarct. The nonprotein nitrogen and the diastolic blood pressure were elevated. This gives strong evidence of frank renal disease. The basal metabolic rate was only -27 per cent. Apparently, no thyroid medication was given. If a total thyroidectomy was actually performed, a rate considerably lower than this would have been expected at this time.

The third admission, four months later, gives us little added data. The patient was still in failure. Her rhythm at the moment was regular.

On the fourth admission, she reported an improved state. For four years, she had been able

to do light housework, up to the evident development of recurrent active rheumatic fever following a respiratory infection. The mitral stenosis was apparently becoming more marked, with a rumbling mitral diastolic murmur. Laboratory studies confirmed the presence of active infection. The urine showed many white cells in addition to albumin, casts and blood cells. In spite of this, the blood pressure was relatively low.

Six months later, the patient re-entered the hospital with congestive failure.

On the sixth admission, four months later, she was again in failure. Surprisingly, there was a normal metabolic rate. There is still no mention of thyroid medication. This strongly suggests that the supposedly totally ablated thyroid gland had regenerated, but she still had hypoparathyroidism. She showed a definite colon-bacillus infection of the urine.

The seventh admission was for further congestive failure. The eighth admission was for treatment of incipient tetany.

The final entry (seven and a half years after the initial entry) was for further congestive failure. The patient had considerable abdominal pain, just where we are not told, but there is little to correlate this with, except for the enlarged, tender liver. She had a rise in temperature and white-cell count. There is no positive evidence on which to say whether this was recurrent rheumatic infection or terminal pulmonary infection, or even urinary infection. The heart had become "enormous." Slow irregular rhythm with coupling indicates a diseased myocardium, if not made toxic with digitalis. We have no details regarding the sudden and unexpected death. A massive pulmonary embolus may have occurred, but there is no positive evidence for this. The patient may very well have had acute cardiac dilatation and standstill, with acute pulmonary edema.

There can be little doubt that this patient had primarily rheumatic heart disease, with chronically recurrent rheumatic fever. She must have developed an extreme degree of mitral stenosis. There was never any evidence of aortic involvement. The tricuspid valve was undoubtedly dilated and incompetent. We may wonder about tricuspid stenosis, but cannot make this as a positive diagnosis. In the treatment of the congestive failure, total thyroidectomy was given a trial. As we read this protocol, we can hardly believe that this procedure accomplished a great deal for the patient, unless it were in prolonging a rather miserable life. I believe we shall find that a full ablation of the gland was not done and that regeneration of functional tissue took place. The

alternate to this may be that aberrant thyroid tissue was present and subsequently hypertrophied. A large part of the parathyroid tissue must have been removed at operation, resulting in a persistent hypoparathyroidism; we may find a scarred portion of one gland remaining. All the visceral organs must have shown an extreme degree of chronic passive congestion from the years of heart failure. We may wonder about cardiac cirrhosis, but chronic ascites toward the end was hardly significant enough to warrant this diagnosis, and the liver remained enlarged. We have evidence for at least one old embolic scar in the left kidney, and similar areas of infarction may have been found in the other organs. I am left wondering about the kidneys. In the later entries, further information regarding nonprotein nitrogen and urinary findings is not given. We know that there had been a urinary infection. Undoubtedly, the kidneys, like the liver, showed an extreme degree of chronic passive congestion, and it is possible that they showed a superimposed chronic pyelonephritis. There may well also have been a focal nephritis.

#### CLINICAL DIAGNOSES

Rheumatic heart disease, with mitral stenosis and regurgitation.  
Tricuspid regurgitation?  
Hypothyroidism.  
Hypoparathyroidism?  
Auricular fibrillation.

#### DR. CLARK'S DIAGNOSES

Rheumatic heart disease: mitral stenosis; aortic and tricuspid involvement (?).  
Cardiac cirrhosis?  
Chronic passive congestion.  
Hypoparathyroidism.  
Regeneration of thyroid gland.  
Pyelonephritis?

#### ANATOMICAL DIAGNOSES

Rheumatic heart disease: mitral stenosis and regurgitation; aortic stenosis, slight; tricuspid regurgitation; pulmonary endocarditis, slight; adhesive pericarditis.  
Chronic passive congestion.  
Cardiac cirrhosis of the liver.  
Hydrothorax, bilateral, slight.  
Ascites.  
Hemorrhagic enterocolitis, acute.  
Partial regeneration and hyperplasia of thyroid gland.  
Partial removal of thyroid and parathyroid glands.

## PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: The essential pathologic lesion in this case was, of course, rheumatic heart disease. As Dr. Clark predicted, there was a high grade of mitral stenosis, and, as he suspected but could not prove, the aortic and tricuspid valves were also involved. There was enough interadherence of the aortic cusp to have produced a slight but definite stenosis, and the chordae of the tricuspid valve were so shortened that there must have been regurgitation. A minimal scarring, without functional deformity, was also noted on the pulmonary valve. Further evidence of a pancarditis was an almost complete fibrous obliteration of the pericardial cavity. Neither in the valves nor in the myocardium could we find any evidence of acute rheumatic infection.

Another suspicion of Dr. Clark's was likewise confirmed. The liver was small, and its surface very finely pebbled; it cut with definitely increased resistance. On microscopic examination, distinct fibrosis of the centers of the lobules was apparent, in addition to the evidence of severe passive congestion. So that the diagnosis of cardiac cirrhosis was confirmed.

The lungs showed little except chronic passive congestion, and the terminal episode proved to have been a diffuse hemorrhagic enterocolitis, which was entirely unexpected. The kidneys were surprisingly normal. They were of course, slightly swollen and congested, but there was no evidence of pyelonephritis, and we did not find any scar of a healed infarct. As Dr. Clark guessed, the thyroidectomy had not been total. A nodule that weighed between 2 and 3 gm. and showed on microscopic examination intense hyperplasia had regenerated. In a search for parathyroid glands, a small fragment of accessory thyroid tissue was found, which was likewise hyperplastic. No parathyroid gland could be identified.

## CASE 27522

## PRESENTATION OF CASE

A fifty-one-year-old Italian laborer was transferred to the Emergency Ward from another hospital because of coma and increasing neurologic signs of thirty-six hours' duration.

Five weeks before admission, the patient became flushed, had chills, began to cough, and complained of pain in the left lower chest. He remained in bed for three days, but did not improve and entered a local hospital, where examination showed crackling rales over the upper left chest, with dullness to flatness below the level

of the left fourth rib. There was marked bronchovesicular breathing in the right chest. An x-ray film showed consolidation in the left lower lobe of the lung. The head and abdomen were normal.

The patient was treated with sulfathiazole, but responded poorly. Subsequent x-ray films showed persistent consolidation in the left base, and an apparent left interlobar mass, which became progressively more prominent. Several chest taps failed to reveal fluid or pus. The temperature spiked between 101 and 105°F. (rectal) for two and a half weeks. Following a four-day course of sulfapyridine, the temperature returned to normal, and there was general improvement in the patient's condition.

Five weeks after onset of the illness, while still in the local hospital, the patient suddenly became apathetic, listless and unresponsive. He developed sphincter incontinence, and in the course of thirty-six hours lapsed into deep coma.

The family history was noncontributory. The patient was a chronic alcoholic.

Physical examination showed a comatose, apparently moribund man who was breathing stertorously but regularly. There was no cyanosis. A leathery rub was heard in the left axilla, and there were scattered rales in the left base. Dullness was evident posteriorly on the left at the level of the fifth and sixth ribs, medial to the scapula. The liver edge seemed firm and smooth and was two fingerbreadths beneath the costal margin. The pupils were round but unequal, and reacted to light. The fundi showed full retinal veins, with initial blurring of the disks. There was a suggestive left central facial weakness. The head was held tilted and rotated to the left, with marked rigidity of the neck. All extremities were hyper-tonic, the right arm more than the left. The tendon reflexes were exaggerated bilaterally although more markedly so on the right. The abdominal reflexes were absent, and the Babinski reflex was positive on both sides.

The heart sounds were rapid and distant. The pulse was 110, the temperature 106°F., and the respirations 40.

Examination of the blood showed a red-cell count of 3,050,000 with a hemoglobin of 50 per cent, and a white-cell count of 21,600 with 93 per cent polymorphonuclears. The urine showed a specific gravity of 1.014, with a +++ test for albumin, no sugar, and only occasional white cells in the sediment. The nonprotein nitrogen of the blood serum was 20 mg. per 100 cc.

A lumbar puncture gave 6 cc. of turbid, later blood-tinged fluid, the pressure falling from 155

to 125 mm. of water. The respiratory and pulse oscillations were normal. The fluid showed a white-cell count of 4670, with polymorphonuclear leukocytes predominating. Gram-positive cocci in pairs and chains appeared on smear. Puncture of the left chest in the fifth interspace, 10 cm. lateral to the spinous process, yielded 45 cc. of sanguinopurulent fluid.

A roentgenogram of the chest showed homogeneous density obliterating the left side of the diaphragm, rising to the fourth rib posteriorly in a thin band. The heart was not displaced. A roentgenogram of the skull was normal.

The patient was continued on sulfapyridine, and a blood level of 13 mg. per 100 cc. was obtained. He was given repeated intravenous fluids and oxygen therapy.

Death occurred on the third hospital day, five and a half weeks after onset of the illness.

#### DIFFERENTIAL DIAGNOSIS

DR. AUGUSTUS S. ROSE: The cause of death in this case was clearly an intracranial infectious process. Meningitis was definitely established, as was the intrapleural infection from which the meningitis ultimately arose. The neurologic problem is therefore confined to the question of the co-existence of a brain abscess.

The terminal illness began with fever, chills, cough and pain in the chest, and physical and x-ray examinations confirmed the suspicion of lobar pneumonia. The consolidation, however, did not clear, and for a time, the patient responded poorly to clinical therapy. At this time, empyema, which was unquestionably present, was suspected, but fluid was not obtained by chest tap. Two and a half weeks later, while apparently convalescing, the patient suddenly became semicomatose, lost sphincter control and grew progressively worse until death three days later.

We are not told of the symptoms that he must have had during the two weeks between the two acute phases of his illness. But thirty-six hours after the onset of coma, physical examination and, indeed, a chest tap revealed the persistence of the empyema. Neurologic examination showed a stiff neck, unequal pupils, distended retinal veins, with a question of early papilledema, a suggestive left central facial weakness, unequal hyperactive reflexes and bilaterally positive Babinski signs. Lumbar puncture showed turbid, blood-tinged spinal fluid, with a white-cell count of 4600 cells and a normal pressure (155 mm. of water). A smear of the fluid showed gram-positive cocci in pairs and chains. The sugar determination would be of interest, but is unnecessary.

On the basis of these facts, we can say the patient had empyema of the left pleura and pneumococcal meningitis. However, does pneumococcal meningitis explain the total picture? Was there a brain abscess that ruptured into a ventricle?

Pneumococcal meningitis may be one of the most fulminating of meningeal infections. Not infrequently, it is ushered in by a convulsion and coma, and if the infection is untreated, death may follow in a day or two. More commonly, however, headache, chills and apathy precede the more dramatic symptoms by some hours. Neurologic signs, as in this case, may also appear in meningitis, because of degenerative changes in the cells of the cortex and brain stem, secondary to the overlying exudate and infection. There is room for doubt whether such widespread damage would occur in thirty-six hours as to produce the signs exhibited by this patient when the spinal-fluid pressure was normal. The pressure is almost universally elevated in severe meningitis. The absence of increased pressure in this case requires explanation. It is also unusual to find blood-tinged spinal fluid in uncomplicated meningitis.

These objections to meningitis (sudden onset, many neurologic signs, normal spinal-fluid pressure and blood-tinged spinal fluid) can be met by the diagnosis of one or more metastatic brain abscesses, with rupture of one into a lateral ventricle. It is possible that a bacteremia occurred during the first or second week of the illness, while the temperature was spiking. The advancing pulmonary infection could have overshadowed symptoms referable to the head. If the cerebral lesion had been located near the ventricular wall, dramatic neurologic signs would not necessarily have developed. Furthermore, it is a frequent clinical observation that a brain abscess may attain considerable size before the development of increased intracranial pressure. The rupture of an abscess into a ventricle almost invariably changes a relatively benign localized infection into a sudden, overwhelmingly malignant one.

#### CLINICAL DIAGNOSES

Pneumonia.  
Empyema.  
Brain abscess.  
Meningitis.

#### DR. ROSE'S DIAGNOSES

Empyema, left pleura.  
Pneumococcal meningitis.  
Brain abscess, ruptured.

conserved. These standards are necessarily high. It is possible that they should be still higher. In any event, the average physician is not familiar with them. He should be, for to him may fall the task of preliminary examination of applicants for one or another branch of the Army or Navy, and on him devolves the task of preventing or correcting, if possible, the defects in selectees or such applicants that disqualify for full military service. In this respect, two articles in this issue of the *Journal*, which deal with the cardiovascular standards for the United States Army and the general physical standards for its aviation cadets, are of particular interest. These standards should even be attained in civilian life, and they could be if the average physician were conversant with them. A better and stronger nation would result—come what may.

"Health is the second blessing that we mortals are capable of, a blessing that money cannot buy"—but wisdom and knowledge may.

## MEDICAL EPONYM

### LOEFFLER'S MEDIUM

The description of the culture medium that still bears his name occurs on page 461 of the monograph by Friedrich August Johann Loeffler (1852-1915), of Berlin, "Untersuchungen über die Bedeutung der Mikroorganismen für die Entstehung der Diphtherie beim Menschen, bei der Taube und beim Kalbe [Studies in the Significance of Micro-organisms in the Occurrence of Diphtheria in Man, in the Pigeon and in the Calf]," which was published in *Mittheilungen aus dem kaiserlichen Gesundheitsamte* (2: 421-499, 1884). A portion of the translation follows:

When the bacilli were sown on the above-mentioned coagulated mixture of 3 parts of calves' or sheep's blood serum and 1 part of neutralized veal broth to which had been added peptone, 1 per cent, glucose, 1 per cent, and sodium chloride, 0.5 per cent, the organisms grew so luxuriantly that at the end of two days there was a whitish coat nearly 1 mm. thick over the surface of the serum, and single colonies had attained an average size of 0.5 cm. In all subsequent trials, therefore, this broth-peptone-glucose serum alone was used as a nutritive base.

R. W. B.

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

#### FATAL SUPPURATIVE UTERINE INFECTION AND PERITONITIS FOLLOWING SELF-INDUCED ABORTION

A twenty-six-year-old unmarried woman was seen at home by her private physician and immediately sent into the hospital. She had passed a fetus five hours previously, and was thought to have been about three months pregnant. Since this was a medicolegal case, the past history was not complete. The patient was reported to have had an illegitimate pregnancy at term three years before the present episode. She was of subnormal mentality, and there was no history of illnesses of any sort.

On entry to the hospital, she had a foul lochia, a subnormal temperature, a pulse of 100 and respirations of 32. Under spinal anesthesia, the patient was curetted, and the uterus swabbed out with iodine. She remained in the hospital only three days and left against advice. During the hospital stay, the temperature did not go above normal.

Two and a half weeks later, she was referred to another hospital by another physician because of acute generalized abdominal pain and vomiting of three days' duration. Examination showed the abdomen to be generally tender, spastic and distended. There was no record of the temperature and pulse, but both were presumably elevated. Blood culture showed a staphylococcus. Sulfanilamide therapy, which had been started, was stopped after the report of the blood culture. The patient died two weeks after entry. Autopsy revealed a septic uterus and an acute suppurative generalized peritonitis.

*Comment.* There is little question that this was a self-induced abortion. This patient was described as being mentally subnormal. Pregnancy in this class of person is a great social problem; abortion is not frequent—much oftener these pregnancies go to term and complicate the social and economic problem for the state.

Although the patient herself was responsible for this death, the treatment that she received on entering the hospital is open to criticism. Conservatism in the handling of all septic abortions

\*A series of selected case histories by members of the section have been published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, Secretary, 330 Dartmouth Street, Boston.

should be followed, this means leaving the uterus absolutely alone, except in the face of hemorrhage. In this case, the curettage was done not because of hemorrhage but because the patient was known to have aborted and still had a foul smelling lochia. Since no temperature reaction followed this intrauterine manipulation, it may well be that the curettage did no appreciable harm, and it is barely possible that had this patient stayed in the hospital, the fatal outcome might have been prevented. In view of the subsequent history and the autopsy findings, sepsis was present in spite of the normal temperature when the patient went home. The diagnosis of peritonitis was so apparent when she entered the second hospital that only conservative treatment was applicable. It would be very helpful to the medical profession if the medical examiners were adamant in performing autopsies in all cases of maternal death that come under their jurisdiction.

If hemorrhage is a complication of septic abortion, it must be controlled, and the retained products, whose presence in the uterus is the cause of the hemorrhage, must be removed. The removal of such products should be done with the greatest care, preferably with the finger and not the curet, and the uterus should be picked to control further bleeding. Acute hemorrhage should be treated by transfusion, and in all septic abortions cultures from the uterus and blood stream should be taken and intelligent chemotherapy instituted. But in the absence of hemorrhage, the uterus should be left alone.

## DEATHS

**DUFFY**—JAMES J. DUFFY, MD, of New York City, died recently. He was in his fifth year.

Born in Webster, Massachusetts, Dr. Duffy received his degree from Harvard Medical School in 1919. He was a former member of the Massachusetts Medical Society.

**FLEMING**—PETER J. FLEMING, MD of Jamaica Plain, died December 15. He was in his sixty-seventh year.

Dr. Fleming received his degree from the University of Western Ontario Medical School in 1902. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow survives him.

**MANNING**—ARTHUR F. MANNING, MD, of Waltham, died December 12. He was in his fortieth year.

Dr. Manning received his degree from Harvard Medical School in 1928. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow survives him.

**MARTIN**—ARCHIBALD H. MARTIN, MD, of Lynn, died December 13. He was in his seventieth year.

Born in Manchester, New Hampshire, Dr. Martin re-

ceived his degree from the College of Physicians and Surgeons, Boston in 1896. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

He is survived by his widow, a daughter and a son.

## DEFENSE ACTIVITIES

### CIVILIAN DEFENSE

#### TRAINING OF VOLUNTEER NURSES' AIDES

The national emergency has brought about a shortage of nurses in hospitals, clinics, public-health and field nursing agencies. To relieve this situation, which is likely to grow more acute with the expansion of military establishments and of plans for civilian defense, the American Red Cross and the Office of Civilian Defense have jointly undertaken a project to train volunteer nurses' aides. With such assistance graduate nurses may extend their services to many more persons. The volunteer aides will work under supervision of a nurse and are being trained for certain nontechnical tasks in order that graduate nurses may be released for the highly technical duties to which alone they are qualified to perform.

The local chief of emergency medical service and the local office of civilian defense in communities where the training program is undertaken have definite responsibilities listed as follows by the national headquarters of the Office of Civilian Defense:

(1) To assist the local Red Cross chapter and the Civilian Defense Volunteer Office in recruiting and enrolling desirable applicants for training.

(2) To assist local chapters to conclude arrangements with appropriate general hospitals to serve as training centers.

(3) To assist the local Red Cross chapter in organizing and maintaining a placement service so that volunteer nurses' aides may continue to serve and to accumulate experience.

(4) To reassign volunteer nurses' aides to emergency duty if the need should arise.

The American Red Cross, in collaboration with the Medical Division of the Office of Civilian Defense, has revised its standard course of instruction for volunteer nurses' aides with reference to needs that may develop during the period of the national emergency. The standard course was instituted in July, 1940, an outgrowth of volunteer services that have been sponsored by the Red Cross since World War I. The first half of the course, consisting of lectures and demonstrations, is given in a Red Cross chapter house or some other suitable place. The second half is given in a hospital selected by the American Red Cross and the Office of Civilian Defense as a training center under strict supervision.

Nurses' aides are to work under supervision of a nurse at all times, never independently, the instructions point out. Moreover, they must agree to serve without remuneration and in time of national peril must be prepared to serve whenever and for as long a period as needed. Authorized duties for the nurses' aides have been outlined in the Red Cross publication, *Chapter Organization and Administration of Red Cross Volunteer Nurses Aide Corps*. These duties are of course subject to approval of individual institutions. In hospitals they may, among other activities, make beds, take care of personal belong-

ings of patients, take care of rubber goods, clean dressing trays, take care of linen closets, feed helpless patients, take patients to and from treatment rooms, help with admission and discharge of patients and care for ambulatory patients. In dispensaries and clinics the aides may serve as interpreters in foreign languages, interpret clinic rules and instructions to patients, help weigh and measure, undress and dress children, assist in taking physicians' notes, help with inventories, clean and put away instruments and help put rooms in order after clinics. In community health agencies the aides may perform whatever nursing duties are approved by the organization for which they work, provided these duties are performed under the direct supervision of a nurse.

## MISCELLANY

### HUNTINGTON MEMORIAL HOSPITAL

Harvard University and the Massachusetts General Hospital have recently announced the conclusion of an agreement by which the main phases of the work in cancer treatment and research now being carried on by the Collis P. Huntington Memorial Hospital will be transferred to the Massachusetts General Hospital. The change will become effective as early in 1942 as possible.

"This step is being taken," the statement said, "in accordance with a long-held belief of both the University and the Massachusetts General Hospital that the care and treatment of medical specialties can be more efficiently handled as part of a large institution of general scope than in smaller individual units. Both the hospitals concerned have been major factors in the study and treatment of cancer in the New England area for many years; and it is confidently believed that the combination of their facilities will not only provide an improved service for patients suffering from malignant disease, but will also render such service more economically to the general community.

"Under the new arrangement, there will be transferred to the Massachusetts General Hospital the inpatient and outpatient services now available at the Huntington Memorial Hospital. By extension of its outpatient service, the Massachusetts General Hospital can readily accommodate all patients who have heretofore been using the Huntington Hospital; during the last year the latter cared for 14,000 outpatient visits. The Massachusetts General Hospital also has ample space in which to set up additional beds to equal the present complement at the Huntington Hospital; hence there will be no reduction in the number of beds available for the care of cancer patients in the community as a result of the change.

"The Laboratory and research work now carried on by the Harvard Cancer Commission through employment of certain funds of Harvard University will continue under supervision of that commission. Research activities under the direction of Dr. Joseph C. Aub will be carried on at the Massachusetts General Hospital in connection with the large and well-organized tumor clinic which that hospital has been operating for many years. The remainder of the varied research work of the Harvard Cancer Commission will be continued in conjunction with the Harvard Medical School.

"The equipment of the Massachusetts General Hospital, including its modern 1,000,000-volt x-ray machine, will be available to all patients, and the Harvard supply of radium, heretofore used at the Huntington Hospital, will be transferred to the Massachusetts General Hospital."

## RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR OCTOBER, 1941

DISEASES	OCTOBER 1941	OCTOBER 1940	FIVE YEAR AVERAGE*
Anterior poliomyelitis	45	7	13
Chicken pox	571	491	367
Diphtheria	9	20	16
Dog bite	902	845	778
Dysentery, bacillary	43	21	43
German measles	35	26	28
Gonorrhea	351	374	455
Measles	373	619	258
Meningitis, meningococcal	10	5	5
Meningitis, other forms	2	—	—
Mumps	335	199	179
Paratyphoid infections	6	3	2
Pneumonia, lobar	192	219	229
Scarlet fever	467	266	291
Syphilis	450	394	430
Tuberculosis, pulmonary	342	223	243
Tuberculosis, other forms	33	30	30
Typhoid fever	11	6	6
Undulant fever	6	3	5
Whooping cough	555	645	491

\*Based on figures for preceding five years

### GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Actinomycosis was reported from Boston, 1; Reading, 1; total, 2.

Anterior poliomyelitis was reported from: Acushnet, 3; Adams, 1; Andover, 1; Boston, 4; Bourne, 1; Brockton, 2; Cambridge, 1; Carver, 1; Chelsea, 1; Danvers, 1; Dedham, 1; Falmouth, 1; Fall River, 1; Lowell, 1; Lynn, 4; Malden, 1; Merrimac, 1; New Bedford, 2; North Attleboro, 1; Norfolk, 1; Pittsfield, 3; Saugus, 1; Southboro, 1; Springfield, 1; Taunton, 2; Wakefield, 1; Walpole, 1; Ware, 2; Wellesley, 1; West Bridgewater, 1; total, 45.

Anthrax was reported from: Holyoke, 1; Springfield, 1; total, 2.

Diphtheria was reported from: Boston, 1; Bourne, 1; Fall River, 6; Worcester, 1; total, 9.

Dysentery, bacillary, was reported from: Adams, 1; Arlington, 1; Boston, 3; Dracut, 2; Ipswich, 5; Lawrence, 1; Lowell, 1; Melrose, 8; Springfield, 1; Worcester, 20; total, 43.

Infectious encephalitis was reported from: Lynn, 1; Springfield, 1; total, 2.

Meningitis, meningococcal, was reported from: Boston, 1; Brockton, 1; Ipswich, 1; Fort Devens, 1; New Bedford, 1; Quincy, 1; Randolph, 1; Waltham, 1; Woburn, 2; total, 10.

Meningitis, other forms, was reported from: Brockton, 1; Taunton, 1; total, 2.

Paratyphoid infections were reported from: Boston, 2; Everett, 1; Fort Devens, 1; Lynn, 1; Malden, 1; total, 6.

Septic sore throat was reported from: Boston, 2; Fall River, 1; Hingham, 1; Medford, 2; New Braintree, 1; Salisbury, 1; Waltham, 1; Weymouth, 1; Williamstown, 1; total, 11.

Tetanus was reported from: Boston, 1; total, 1.

Trachoma was reported from: Boston, 1; Dedham, 1; Lynn, 1; total, 3.

Trichinosis was reported from: Attleboro, 1; Boston, 1; total, 2.

Typhoid fever was reported from: Boston, 3; Brockton, 1; Cambridge, 1; Fall River, 1; Fitchburg, 1; Norwood, 1; Springfield, 1; Westwood, 1; Worcester, 1; total, 11.

Undulant fever was reported from: Great Barrington, 1; Mendon, 1; North Adams, 1; Worcester, 3; total, 6.

Anterior poliomyelitis continued at a level above the usual seasonal incidence of nonepidemic years.



Chicken pox, dog bite and mumps showed record high incidences, this being the second consecutive month for dog bite and the fourth for mumps.

Scarlet fever had the highest prevalence for October since 1935.

German measles, measles, meningococcal meningitis, paratyphoid infections, pulmonary tuberculosis, typhoid fever, and whooping cough were reported above the five year averages.

Diphtheria and lobar pneumonia were reported below the five year averages.

The incidences of bacillary dysentery and undulant fever were not remarkable.

## NOTE

The election of Dr George R Minot, professor of medicine at Harvard Medical School, as president of the Inter State Postgraduate Medical Association of North America was recently announced.

## CORRESPONDENCE

### HEALTH OF THE WORKER AND HIS FAMILY

To the Editor: I noted with great interest and satisfaction the inclusion in the December 11 issue of the *Journal* of an article by Mr Bloomfield entitled "The Private Physician's Opportunity in Industrial Medicine" and another by Dr Pinto and Mr Bowditch entitled "Industrial Medicine." Also, your board saw fit to devote an editorial to this subject.

We have been frequently reminded that the present war is different from any other in which we have ever engaged and that there are two fronts that defended by the armed forces and that supported by civilians, the most important of whom are those engaged in defense industries. There is a degree of satisfaction in this latter point, since every person has a definite sense of playing his part in winning the war and defending the freedoms for which we are fighting. Today, the boy who is found physically unfit for service, but who is by no means an invalid, can hold his head high with the sense that he has a duty and a service to perform that is second only to the man at the front. This is also true of older people and of women, and it is going to require the full measure of effort of a determined people, physically fit and with a high war morale, to win out against our powerful and treacherous foes.

Industrial hygiene is not a new field. Those concerned with this work, however, have quite generally been interested only in those diseases or injuries that arise because of certain inherent conditions within a particular industry. We are reminded by Mr Bloomfield's article that there is enormous waste of life and efficiency resulting from nonindustrial illness among workers. It is estimated that of the 400,000,000 man-days a year lost because of disabilities, only 5 or 10 per cent can be classified as due to specific industrial hazards. The major problem has to do, obviously, with the various forms of illness, such as respiratory infections, gastrointestinal disease and the like, that occur in all people but show in excess, oftentimes, among industrial workers. It is a familiar fact that disease prevalence varies inversely with income when this is below a certain level. We know that women in industry suffer from an excess of absenteeism six times that of men. If we are really going to make a contribution to the war effort, the greatest opportunity lies in the field of reducing the common illnesses of man.

I am not, in this, belittling the value of setting up the necessary safeguards against chemical poisonings, dust hazards, physical injury and other specific industrial diseases, but I am saying that we must change the general philosophy that has prevailed and look realistically at the relative values of our efforts in this field and that employers, employees, industrial physicians, private physicians, industrial nurses and all the rest of us must adopt a new point of view. There are the same possibilities of reducing sickness among the industrial workers who congregate together daily as there are in prevailing diseases in the general community. The field is as broad as the whole public health program.

To study ways and means of assisting and furthering a complete industrial hygiene program, the Health Division of the Massachusetts Committee on Public Safety has created the Committee on Occupational Hygiene, which comprises representatives from the Massachusetts Medical Society, employers, employees, industrial nurses, insurance companies, the health-education group and the Massachusetts Division of Industrial Hygiene. It is hoped that they may bring forth a program that will be constructive and helpful to all concerned in reducing the wastage of manpower resulting from all forms of preventable diseases among the laboring classes.

CURTIS M. HILLIARD, *Director*

Health Division Massachusetts Committee on Public Safety  
18 Fremont Street  
Boston

## REPORTS OF MEETINGS

### PLYMOUTH DISTRICT MEDICAL SOCIETY

A regular meeting of the Plymouth District Medical Society was held November 13 at the Plymouth County Hospital at 11 15 am. The meeting was called to order by the president Dr G A Moore. The minutes of the previous meeting were read by the secretary, Dr R C McLeod. Mention was made of the death of Dr H H Burns, of Plymouth, in May, 1941.

Dr Bradford Peirce presented a program of films and slides of tuberculous patients treated at the South Hanover Hospital by modern methods, including lobectomy, pneumonectomy, thoracoplasty and pneumolysis. These were illustrated by several cases with recovery. Dr Moore made comment on the vastly improved death rate in tuberculosis in the past thirty years, attributing at least part of the improvement to surgical intervention, and touched lightly on lobectomy and pneumonectomy, which are reserved for well selected cases, he added that, as a rule, the operative results are excellent.

The main speaker was Dr J C McCann, of Worcester, chairman of the Committee on Medical Care Costs Insurance. He gave an outstanding and vigorous plea for co operation by all members of the society, which was well received.

EDWARD S. PERRY, M.D., *Reporter*

### MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY

Dr James C. McCann of Worcester, chairman of the special committee concerned with prepayment medical care costs insurance, spoke at a meeting of the Middlesex South District Medical Society on December 10.

The members of the society passed a resolution, made

by Dr. Charles E. Mongan, that supported the work of Dr. McCann and his committee. It was requested that this fact be published in the *New England Journal of Medicine*.

ALEXANDER A. LEVI, *Secretary*

## BOOK REVIEWS

*The Care of the Aged (Geriatrics)*. By Malford W. Thewlis, M.D. Third edition, entirely rewritten. 8°, cloth, 579 pp., with 50 illustrations. St. Louis: The C. V. Mosby Company, 1941. \$6.00.

The author's long interest in old people is shown by the fact that he has rewritten this book, which first appeared in 1919. It consists of thirty-eight chapters grouped in five sections, and it claims to be "still the only recent book dealing with the medical care of the aged."

The first section, "General Considerations," sketches the value of old-age hygiene, the prevention of premature senility, prolongation of life, work for the aged, hobbies, economic problems and medicolegal relations. Many interesting observations are found, but in general the reviewer believes that the discussion suffers both from incompleteness and from repetition. Exercise is disposed of in five lines. Recreation is given one paragraph, as follows: "Recreation is an important factor. The aged brain becomes fatigued easily; a sophisticated play or film, which causes mental strain should be avoided. The senescent mind reacts well to something lively and humorous." Heredity is discussed in several places. Furthermore, it is not always clear whether the author is thinking of the normal person of sixty, seventy or ninety, of the institutionalized pauper or of the senile dement.

The second section, "Miscellaneous Medical Problems," includes chapters on nutrition, nursing and therapeutics. The chapters on anatomic and pathologic changes in old age suffer seriously on comparison with the scholarly reports in Cowdry's *Problems of Ageing*. The third and fourth sections deal with infectious and noninfectious diseases (the latter are defined as allergy, alcoholism and focal infections).

In the fifth section, "Pathologic Conditions in Old Age," there are subtitles for practically every condition dealt with in standard textbooks of medicine and surgery, with numerous references to medical literature. Statements concerning the changes imposed by age on disease and on its treatment are often given as impressions and as recollections of individual cases drawn from a rich experience. They show good clinical judgment for the most part. Careful reading and rereading, however, leaves one wishing that there were more evidence of critical study and correlation.

The book cannot be highly recommended, since it is not a satisfactory guide to the care of the aged. On the road to geriatrics, it is "a landmark, not a guide post."

*Natural Resistance and Clinical Medicine*. By David Perla, M.D. and Jessie Marmorston, M.D. 4°, cloth, with 1344 pp. and 44 tables. Boston: Little, Brown and Company, 1941. \$10.00.

This is a curious book. Its authors for some time have evidently been interested in what resistance to disease may be, and here, as they say, they have attempted to put down in print an analysis of many of the factors that are believed to determine or modify natural or acquired susceptibility to infection.

The task of putting together such a book is enormous. The authors quote more than five thousand references to

current literature in the forty-six chapters that make the volume. Almost every conceivable phase of resistance to disease is discussed, from the prevention and treatment of surgical shock to the role of copper, iron or manganese to resistance, or from the effect of psychic factors to the effect of age and sex, of endocrine glands or of vitamins.

This is the kind of medical text that one would expect to find in a library—useful for reference or to encourage browsing. It can have very little general appeal to students or practicing doctors. It deserves praise, however, as being an honest effort toward gathering a large conglomeration of literature and crystallizing therefrom a number of stimulating ideas.

New England readers may be interested to know that this is the first large American medical publication to be printed by Little, Brown and Company of Boston. For a book so large, its physical characteristics are handsome. It weighs no more than it has to for its size; the typography is admirable; the indexing is adequate; the illustrations and tables are clear. The appearance of the book, therefore, carries on the fine tradition of expert book making upheld for so many years by its publishers.

*The Principles and Practice of Ophthalmic Surgery*. Edmund B. Spaeth, M.D. Second edition, thoroughly revised. 8°, cloth, with 1149 illustrations and 6 colored plates. Philadelphia: Lea and Febiger, 1941. \$10.00.

Effective surgery is consummated only when a comprehensive diagnosis is combined with surgical skill and ingenuity. In the field of ophthalmology, the internist, neurologist and the ophthalmologist find a common diagnostic meeting ground. The author of this book wisely recognizes the importance of diagnosis, and he incorporates diagnostic considerations as the prerequisite for the choice and application of surgical therapy. The text carries authors' index, as well as a general index.

Lucid writing, a wealth of well-chosen illustrations freely given credits to authorities in their respective fields make this book the collective voice of modern work everywhere, and an indispensable guide for every current practitioner of eye surgery. The twenty-six chapters of the book deal with anesthesia, reconstructive plastic surgery of the eyelids and socket, surgery of the lacrimal apparatus, surgery of the ocular muscles, cataract surgery, glaucoma surgery, reattachment of a separated retina, extraction of intraocular foreign bodies and treatment of radium and surgery of neoplasms of the eye and adnexa.

*A Textbook of Ophthalmology*. By Sanford R. Gifford, M.D. Second edition, revised. 8°, cloth, 470 pp., with 255 illustrations and 14 colored plates. Philadelphia: W. B. Saunders Company, 1941. \$4.00.

The second edition of Gifford's excellent work corrects the typographic errors of the first edition, and is reprinted with many informative illustrations in black and white and in color. The author has rewritten portions of the book to cover advances in knowledge that have taken place since the publication of the first edition, notably in chemotherapy as applied to ophthalmology, and in the ophthalmic manifestations of general diseases.

The practitioner and the medical student will find here concise, interesting and dependable information to guide them in understanding how to deal with the ophthalmic problems that arise in practice.

